

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date  
24 June 2004 (24.06.2004)

PCT

(10) International Publication Number  
**WO 2004/053057 A2**

- (51) International Patent Classification<sup>7</sup>: C12N
- (21) International Application Number: PCT/US2003/034563
- (22) International Filing Date: 31 October 2003 (31.10.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
60/432,651 11 December 2002 (11.12.2002) US
- (71) Applicant: 3M INNOVATIVE PROPERTIES COMPANY [US/US]; 3M Center, Post Office Box 33427, Saint Paul, MN 55133-3427 (US).
- (72) Inventors: GUPTA, Shalley K.; Post Office Box 33427, Saint Paul, MN 55133-3427 (US). GHOSH, Tarun K.; Post Office Box 33427, Saint Paul, MN 55133-3427 (US). FINK, Jason R.; Post Office Box 33427, Saint Paul, MN 55133-3427 (US).
- (74) Agents: GRAM, Christopher D., et al.; Office of Intellectual Property Counsel, Post Office Box 33427, Saint Paul, MN 55133-3427 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT (utility model), AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ (utility model), CZ, DE (utility model), DE, DK (utility model), DK, DM, DZ, EC, EE (utility model), EE, EG, ES, FI (utility model), FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK (utility model), SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

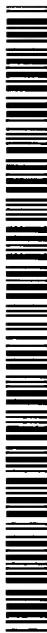
Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for all designations
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations

Published:

- without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



WO 2004/053057 A2

(54) Title: GENE EXPRESSION SYSTEMS AND RECOMBINANT CELL LINES

(57) Abstract: The present invention provides gene expression systems useful for detecting agonists of Toll-like receptors. The gene expression systems include a nucleic acid sequence encoding a Toll-like receptor and a second nucleic acid sequence that encodes a reporter operably linked to an expression control sequence. The recombinant cell lines include a gene expression system according to the present invention.

**GENE EXPRESSION SYSTEMS AND RECOMBINANT CELL LINES****Background of the Invention**

Cells of the immune system secrete a diverse set of compounds including cytokines, chemokines, co-stimulatory markers, and defensins in response to an immunological challenge.

Certain compounds known as immune response modifiers ("IRMs") possess potent immunostimulating activity including but not limited to antiviral and antitumor activity. Certain IRMs effect their immunostimulatory activity by, e.g., inducing the production and secretion of certain cytokines while inhibiting production and secretion of other cytokines. Certain IRMs are small organic molecules such as those disclosed in, for example, U.S. Patent Nos. 4,689,338; 4,929,624; 5,266,575; 5,268,376; 5,352,784; 5,389,640; 5,482,936; 5,494,916; 6,110,929; 6,194,425; 4,988,815; 5,175,296; 5,367,076; 5,395,937; 5,693,811; 5,741,908; 5,238,944; 5,939,090; 6,245,776; 6,039,969; 6,083,969; 6,245,776; 6,331,539; and 6,376,669; and PCT Publications WO 00/76505; WO 00/76518; WO 02/46188, WO 02/46189; WO 02/46190; WO 02/46191; WO 02/46192; WO 02/46193; and WO 02/46194.

Additional small molecule IRMs include purine derivatives (such as those described in U.S. Patent Nos. 6,376,50 and 6,028,076), small heterocyclic compounds (such as those described in U.S. Patent No. 6,329,381), and amide derivatives (such as those described in U.S. Patent No. 6,069,149).

Other IRMs include large biological molecules such as oligonucleotide sequences. Some IRM oligonucleotide sequences contain cytosine-guanine dinucleotides (CpG) and are described, for example, in U.S. Patent Nos. 6,1994,388; 6,207,646; 6,239,116; 6,339,068; and 6,406,705. Other IRM nucleotide sequences lack CpG and are described, for example, in International Patent Publication No. WO 00/75304.

Some of these IRMs induce cellular responses (e.g., the production and/or secretion of cytokines, chemokines, etc.) through one or more Toll-like receptors (TLRs). For example, certain small organic molecule IRMs are agonists of one or more of TLR-1, TLR-2, TLR-4, TLR-6, TLR-7, and TLR-8. Additionally, CpG has been reported to act through TLR 9.

In certain cells of the immune system, TLR activation can be associated with activation of the transcription factor NF- $\kappa$ B. NF- $\kappa$ B activation is associated with certain cellular responses to an immunological challenge, such as the production and secretion of pro-inflammatory cytokines such as TNF- $\alpha$ , IL-1, IL-6, IL-8, IL-10, IL-12, MIP-1, and MCP-1. IRM induction of such cellular responses can be demonstrated by measuring activation of the transcription factor NF- $\kappa$ B in response to exposing a cell to an IRM compound (See, e.g., Chuang *et al.*, *Journ. of Leuk. Biol.*, vol. 71, pp. 538-544 (2002), and Hemmi *et al.*, *Nature Immunology*, vol. 3(2), pp. 196-200 (2002)). Thus, NF- $\kappa$ B activation can be used as a reporter of TLR activation. However, the extent of NF- $\kappa$ B activation does not necessarily correlate with the extent of the downstream cellular response. This is so because the downstream cellular response may be modulated by one or more additional factors.

#### Summary of the Invention

The present invention provides an expression system that includes a first nucleic acid sequence that encodes a Toll-like receptor operably linked to a first expression control sequence; and a second nucleic acid sequence that encodes a reporter that (a) generates a detectable signal when the reporter is expressed and the cell is exposed to conditions effective for generating the detectable signal, and (b) is operably linked to a second expression control sequence that comprises a cytokine promoter, a chemokine promoter, a co-stimulatory marker promoter, or a defensin promoter. In some embodiments, the first nucleic acid sequence and the second nucleic acid sequence are included on a single vector. In other embodiments, the first nucleic acid sequence and the second nucleic acid sequence are located on separate vectors.

In another aspect, the present invention provides a recombinant cell line that includes a host cell transfected with an expression system. In some embodiments, the expression system is contained within a single vector. In other embodiments, the expression system is contained among two or more vectors so that the host cell is co-transfected with all of the vectors of the expression system to obtain the recombinant cell line. In one embodiment, the host cell is a Namalwa cell.

In another aspect, the present invention provides a TLR agonist identified using either an expression system or a recombinant cell line according to the present invention.

In yet another aspect, the present invention provides pharmaceutical compositions including a TLR agonist identified using either an expression system or a recombinant cell line according to the present invention.

Various other features and advantages of the present invention should become  
5 readily apparent with reference to the following detailed description, examples, and appended claims. In several places throughout the specification, guidance is provided through lists of examples. In each instance, the recited list serves only as a representative group and should not be interpreted as an exclusive list.

10

#### Detailed Description of Illustrative Embodiments of the Invention

The present invention provides gene expression systems and recombinant cell lines that may be useful for detecting TLR activation based on detecting induction of a downstream cellular response to TLR activation (e.g., production or secretion of one or more immune system compounds such as cytokines or co-stimulatory markers) rather than NF- $\kappa$ B activation. In some cases, the cellular response may be mediated by NF- $\kappa$ B, but in other cases the cellular response may be NF- $\kappa$ B-independent. Thus, the present invention provides gene expression systems and recombinant cell lines that may be useful for detecting a broader range of TLR activation than is possible by monitoring NF- $\kappa$ B activation. This may provide an ability to identify certain TLR agonists that would not be detected using an assay based on NF- $\kappa$ B activation. The gene expression systems and recombinant cell lines of the present invention also may provide a more relevant indication of the quantitative character of a particular cellular response to TLR activation by a particular TLR agonist.  
15  
20

In some cases, a gene expression system or recombinant cell line according to the present invention may be useful for detecting TLR activation that is not accompanied by NF- $\kappa$ B activation. Accordingly, the gene expression system and recombinant cell line may be employed to identify TLR agonists that do not necessarily also activate NF- $\kappa$ B. Such TLR agonists may be useful for treatment or prevention of certain conditions in which the production and secretion of pro-inflammatory cytokines such as those induced by NF- $\kappa$ B activation may be undesirable.  
25  
30

For purposes of this invention, the following terms shall have the meanings set forth.

“Activation” refers to modifying the indicated protein so that the protein provides a biological function. For example, TLR activation refers to modifying a TLR - for example, a conformational modification such as in response to exposure of the TLR to an agonist - so that the TLR is capable of inducing the production and secretion of certain cytokines.

“Agonist” refers to a compound that can combine with a receptor (e.g., a TLR) to produce a cellular response. An agonist may be a ligand that directly binds to the receptor. Alternatively, an agonist may combine with a receptor indirectly by, e.g., (a) forming a complex with another molecule that directly binds to the receptor, or (b) otherwise results in the modification of another compound so that the other compound directly binds to the receptor. An agonist may be referred to as an agonist of a particular TLR (e.g., a TLR6 agonist).

“Amino acid sequence” refers to a particular ordered sequence of amino acids, whether naturally occurring or engineered.

“Co-transfect” and variations thereof refer to transfecting a host cell with more than one vector. A host cell may be co-transfected by transfecting with two or more vectors one at a time or in any convenient combination of vectors, including simultaneous transfection with all vectors.

“Express” and variations thereof refer to the ability of a cell to transcribe a structural gene to mRNA, then translate the mRNA to synthesize a protein that provides a detectable biological or biochemical function. “Expressible” refers to the ability of a particular nucleic acid sequence to be expressed by a cell that contains the nucleic acid sequence.

“Immune system compound” refers to any compound that is produced or secreted by cells of the immune system in response to an immunological challenge. Immune system compounds include but are not limited to cytokines, chemokines, co-stimulatory markers, and defensins.

“IRM compound” refers to a compound that alters the level of one or more immune system compounds when administered to an IRM-responsive cell. Representative IRM compounds include the small organic molecules, purine derivatives, small heterocyclic compounds, amide derivatives, and oligonucleotide sequences described above.

“Nucleic acid sequence” refers generally to a region of DNA that has a definable function such as (a) encoding a peptide, polypeptide, or protein or (b) controlling expression of a nucleic acid sequence that encodes a peptide, polypeptide, or protein. For example, a nucleic acid sequence that encodes TLR6 refers generically to any sequence of 5 nucleotides that encodes a TLR6 protein, without regard to (a) the species source of the nucleic acid sequence, (b) specific nucleotide sequence variants, or (c) whether such nucleotide sequence variants are naturally occurring or engineered.

“Nucleotide sequence” refers to a particular ordered sequence of nucleotide bases, whether naturally occurring or engineered.

10 It has been found that induction of certain secreted proteins or polypeptides can be useful as reporters of TLR activation. For example, IFN- $\alpha$  is a cytokine secreted by such immune system cells as T lymphocytes, macrophages, plasmacytoid monocytes, dendritic cells, and natural killer cells. IFN- $\alpha$  is involved in regulating a host's innate and adaptive immune responses to an immunological challenge, perhaps by providing a link between 15 the two responses [Brassard *et al.*, *Journal of Leukocyte Biology* 71: 565-581 (2002)]. The innate immune response can include the cell-mediated response of natural killer (NK) cells to a non-self (e.g., neoplastic) or foreign (e.g., viral) antigen. IFN- $\alpha$  also may indirectly regulate the balance between Th1 and Th2 cell populations and, therefore, the innate and adaptive immune responses. Moreover, induction of IFN- $\alpha$  is independent of NF- $\kappa$ B 20 activation.

Additionally, the production and secretion of NF- $\kappa$ B-dependent cytokines can be useful as reporters of cellular responses resulting from immunological challenge. Detection and measurement of such cytokines may provide comparative qualitative data regarding a cell's response to immunological challenge that is more relevant to an 25 investigator than NF- $\kappa$ B activation data.

Thus, in certain embodiments, the present invention relates to recombinant cell lines and gene expression systems designed to assist detecting induction of immune system compounds and identification of compounds that induce expression of immune system compounds through TLRs.

30 Parts of the following description are provided in the context of IFN- $\alpha$  induction and detection. However, many of the features of the embodiments described below also may be realized using expression systems and recombinant cell lines designed to

specifically detect or induce other immune system compounds. Thus, expression systems and recombinant cell lines designed to specifically detect or induce immune system compounds other than IFN- $\alpha$  are explicitly included in the scope of the present invention.

The present invention provides a recombinant cell line capable of inducing gene expression from an expression control sequence of a gene that encodes an immune system compound (e.g., IFN- $\alpha$ ) in response to TLR activation. In some embodiments, for example, cells of the recombinant cell line, when exposed to a TLR agonist, can induce expression from an IFN- $\alpha$  promoter to a greater extent than cells of the corresponding untransfected cell line. Cells of the untransfected cell lines may substantially lack a functional level of TLR expression (i.e., untransfected cells may not detectably induce expression from the IFN- $\alpha$  promoter in response to exposure to a TLR agonist). Alternatively, cells of the untransfected cell line may exhibit a baseline level of background TLR function, but the baseline level is less than the level of TLR function observed in cells of the corresponding recombinant (i.e., transfected) cell line.

Cells of the recombinant cell lines include a first nucleic acid sequence that encodes a TLR operably linked to an expression control sequence. The cells also include a second nucleic acid sequence that encodes a reporter capable of generating a detectable signal when it is expressed in the recombinant cell under conditions suitable for generating the detectable signal. The reporter is linked to a second expression control sequence that is capable of being induced by activation of the TLR encoded by the first nucleic acid sequence.

The TLR encoded by the first nucleic acid sequence may be any TLR. Ten different human TLRs have been identified, cloned, and sequenced. TLRs also are known to exist in other mammals including, for example, mice and chimpanzees. The nucleotide sequences of the ten human TLRs and many non-human TLRs are known, have been published, and are readily accessible from various sequence databases including GenBank. The first nucleic acid sequence may include the nucleotide sequence of any one of the TLRs, whether human or non-human. In one embodiment, the TLR is human TLR6; in another embodiment, the TLR is human TLR7. Alternatively, the first nucleic acid may encode any one of the ten human TLRs, any non-human TLR, or any combination of two or more TLRs that may be desirable for a particular construct.

The first nucleic acid sequence can include a nucleotide sequence that differs from a specific published nucleotide sequence for the TLR encoded by the first nucleic acid sequence. For example, the first nucleic acid sequence can contain one or more substitutions (compared to a published TLR nucleotide sequence) that do not alter the 5 amino acid sequence of the TLR protein expressed from the first nucleic acid sequence. Such a substitution may be termed a degenerate substitution. Nucleotide sequences containing one or more degenerate substitutions compared to a known TLR nucleotide sequence are explicitly included within the scope of nucleotide sequences suitable for use within the first nucleic acid sequence.

10 As another example, certain nucleotide substitutions may alter the amino acid sequence of the TLR protein. For certain amino acid substitutions, however, the chemical properties of the protein having the altered amino acid sequence are similar to the chemical properties of the protein having the native amino acid sequence. Amino acids may be divided into four groups based on the chemical characteristics of the amino acid 15 side groups: neutral, non-polar amino acids include glycine, alanine, valine, isoleucine, leucine, phenylalanine, proline, and methionine; neutral, polar amino acids include serine, threonine, tyrosine, tryptophan, asparagine, glutamine, and cysteine; acidic amino acids include aspartic acid and glutamic acid; and basic amino acids include lysine, arginine, and histidine. Substitution of one amino acid for another amino acid within the same 20 group may have little or no functional effect on the resulting protein because of the similarity of the chemical characteristics of the amino acids involved in the substitution. Such amino acid substitutions may be termed a conservative amino acid substitution. Nucleotide sequences that, when compared to a known TLR nucleotide sequence, generate one or more conservative amino acid substitutions are explicitly included within the scope 25 of nucleotide sequences suitable for use within the first nucleic acid sequence.

The nucleic acid that encodes a TLR may be cloned into an expression vector so that it is under the expression control of its own promoter, a homologous TLR promoter, or any heterologous promoter inducible in an appropriate host cell. For example, in certain embodiments, the TLR6 structural gene may be cloned into the commercially 30 available mammalian expression vector pCI-neo. In this case, the TLR6 structural gene may be cloned into the vector's cloning region using the NheI and MluI restrictions sites. In such an embodiment, after transfection of the vector into a mammalian cell, the TLR6

structural gene is under the transcriptional control of the vector's CMV enhancer/promoter region.

The second nucleic acid sequence encodes a reporter that is capable of generating a detectable signal when expressed in a host cell under conditions appropriate for generating the desired detectable signal. A wide variety of suitable reporter systems are known. For example, luciferase gene expression may generate a detectable luminescent signal under appropriate conditions. As another example,  $\beta$ -galactosidase expression can generate a detectable color change under appropriate conditions. As yet another example, production and secretion of an immune system compound may be detected by an enzyme-linked immunosorbent assay (ELISA). These and other reporter systems are known and assays for generating the detectable signals are commercially available.

The second nucleic acid sequence is operably linked to a second expression control sequence that includes a promoter sequence selected to be inducible by activation of the TLR encoded by the first nucleic acid sequence. Thus, expression and activation of the TLR encoded by the first nucleic acid sequence will induce gene expression from the second expression control sequence, thereby causing expression of the reporter, which may be detected by performing an assay designed to detect expression of the reporter. The second expression control sequence may include any suitable nucleotide sequence that can induce expression (e.g., a promoter) of a structural gene upon activation of the TLR encoded by the first nucleic acid sequence. Nucleotide sequences suitable for use as second expression control sequences include promoter sequences of TLR-inducible genes including but not limited to genes encoding cytokines, chemokines, co-stimulatory markers, and defensins. In certain embodiments, the second expression control sequence can include an IFN- $\alpha$ 1 promoter. When the reporter system being employed to detect TLR activation includes detecting production and secretion of an immune system compound with an appropriate ELISA assay, the second expression control sequence may include the promoter of the gene encoding the immune system compounds being expressed and detected as the reporter. However, in certain embodiments, it may be desirable to express the immune system compound from a heterologous promoter.

The first nucleic acid sequence and the second nucleic acid sequence may be contained within a single vector. Alternatively, the first nucleic acid sequence and the second nucleic acid sequence may be on separate vectors and co-transfected into a suitable

host cell. In certain embodiments, for example, the first nucleic acid sequence may be cloned into the pCI-neo vector as described above, while the second nucleic acid sequence can be cloned into a reporter vector. One example of a commercially available reporter vector is the pGL3-Enhancer vector, which includes a luciferase reporter gene downstream 5 of a cloning site for cloning a promoter sequence of interest. In some embodiments, the promoter of a TLR-inducible immune system compound may be cloned into the pGL3-Enhancer cloning site. In one such embodiment, the IFN- $\alpha$  promoter may be cloned into the pGL3-Enhancer cloning site.

10 Suitable host cells include any transfectable cells capable of expressing exogenous mammalian genes. In some embodiments, the host cells may be mammalian cells such as human cells or mouse cells. For example, suitable host cells include human cells or descendants of a human cell including but not limited to Namalwa cells or HEK293 cells. Alternatively, the host cells may be mouse cells or descendants of a mouse cell including but not limited to RAW 264.7 cells.

15 In one embodiment, the host cells include Namalwa cells. Namalwa cells have certain characteristics that may be particularly desirable for certain embodiments of the present invention. For example, Namalwa cells can include an expressible chromosomal IFN- $\alpha$  gene locus. Thus, upon appropriate stimulation (e.g., viral infection), Namalwa cells can be induced to produce and secrete IFN- $\alpha$  from the chromosomal IFN- $\alpha$  gene 20 locus. However, Namalwa cells do not naturally express certain TLRs (e.g., TLR6, TLR7, or TLR9). Certain agonists of such TLRs have been shown to induce IFN- $\alpha$  expression in other cell types (e.g., PMBCs), but may not induce IFN- $\alpha$  expression in Namalwa cells unless a functional level of TLR expression is provided.

25 Namalwa cells transfected with an expression system according to the present invention may be capable of expressing a functional level of the TLR provided by the expression system. Thus, Namalwa cells transfected with an expression system according to certain embodiments of the present invention may inducibly express IFN- $\alpha$  as a result of activating the cloned TLR (e.g., by exposure of the transfected Namalwa cells to an agonist). Thus, certain transfected cell lines of the present invention provide an ability to 30 detect a TLR agonist by detecting TLR-mediated IFN- $\alpha$  expression by Namalwa cells. Such IFN- $\alpha$  expression may occur from the chromosomal IFN- $\alpha$  gene or from an IFN- $\alpha$  promoter cloned into the reporter vector.

Namalwa cells transfected with an expression system according to certain embodiments of the present invention can provide alternative means of detecting TLR expression. First, transfected Namalwa cells may generate a detectable signal as a result of expressing the reporter from the second expression control sequence, which may or 5 may not include an IFN- $\alpha$  promoter (see Table 2). Second, transfected Namalwa cells may produce and secrete IFN- $\alpha$  from the chromosomal IFN- $\alpha$  gene locus. A transfected Namalwa cell line according to the present invention may be used to screen compounds in order to identify those compounds that induce TLR expression, i.e., TLR agonists.

Therefore, the present invention also provides TLR agonist compounds identified 10 using an expression system or a recombinant cell line according to certain embodiments of the present invention. As described above, the expression systems and recombinant cell lines may provide the ability to identify TLR activation that may not be detectable using previously known TLR activation assays. A compound that induces TLR activity detectable by using a gene expression system or a recombinant cell line according to the 15 present invention may be considered a TLR agonist. Such TLR agonists may include chemical structures similar in certain respects to the chemical structures of known IRM compounds. Alternatively, a gene expression system or a recombinant cell line according to the present invention may provide a tool for the screening (e.g., high throughput screening) chemically diverse compounds that may lead to the discovery of new TLR 20 agonists, some of which may contain new chemical core structures capable of activating TLRs.

The present invention also provides pharmaceutical compositions containing a 25 TLR agonist identified using an expression system or a recombinant cell line according to the present invention, or a pharmaceutically acceptable salt thereof, in an amount effective for inducing a TLR-mediated cellular response.

#### Examples

The following examples have been selected merely to further illustrate features, advantages, and other details of the invention. It is to be expressly understood, however, 30 that while the examples serve this purpose, the particular materials and amounts used as well as other conditions and details are not to be construed in a matter that would unduly limit the scope of this invention.

### Construction of vectors

The vector pIFN- $\alpha$ 1-luc was constructed by inserting BglII sites at both ends of the human IFN- $\alpha$ 1 promoter (SEQ ID NO:21). The BglII sites were inserted into the IFN- $\alpha$ 1 promoter and the sequence was amplified using the primer pair of SEQ ID NO:22 and SEQ ID NO:23. The amplified IFN- $\alpha$ 1 promoter was cloned into the pGL3-Enhancing vector (Promega Corp., Madison, WI) at its BglII site.

The vector pCI-TLR6 was constructed by inserting SEQ ID NO:11 (GenBank Accession No. NM 006068), which includes the human TLR6 coding sequence, into the pCI-neo mammalian expression vector (Promega Corp.) at the vector's NheI and MluI restriction sites.

### Transfections

Unless otherwise indicated, all incubations were performed at 37°C with 5% CO<sub>2</sub> at 98% humidity.

Culture medium was prepared from complete RPMI 1640 medium (BioSource International, Inc., Camarillo, CA). Fetal bovine serum (Atlas Biologicals, Inc., Ft. Collins, CO) was added to a final concentration of 7.5% (vol/vol); L-glutamine (BioSource International, Inc.) was added to 5 mM; and sodium pyruvate (BioSource International, Inc.) was added to 1 mM.

Burkitt's Lymphoma lymphoblastoid Namalwa cells (ATCC Accession No. CRL-1432) were grown by incubation in culture medium overnight. Cells were harvested by centrifugation in a tabletop centrifuge (1200 RPM for 5 minutes), and then resuspended in phosphate buffered sucrose to a concentration of 1.3x10<sup>7</sup> cells per milliliter.

For each transfection, a 750  $\mu$ L aliquot of the cell suspension was placed in an electroporation cuvette with 4 mm gaps. 10  $\mu$ g of the pIFN- $\alpha$ 1-luc vector and 10  $\mu$ g of the pCI-TLR6 vector were added to the electroporation cuvette. The cell and vector mixtures were incubated at room temperature for 5 minutes. The cells were electroporated using a BioRad Gene Pulser (BioRad Laboratories, Hercules, CA) set to at 500  $\mu$ F capacitance and 0.27 volts, then incubated at room temperature for 5 minutes.

The electroporated cells were suspended in 10 mLs of culture medium and incubated overnight. Dead cells and debris were removed after 24 hours using a MACS

Dead Cell Removal kit (Miltenyi Biotec, Auburn, CA). Cells were resuspended in 10 mLs of culture medium and incubated for an additional 24 hours.

Transfected cells were selected by adding G418 (Promega Corp., Madison, WI) to a final concentration of 1 mg/mL and incubating the cells for seven days.

5

### Assays

The selected transfected cells were counted and resuspended to a concentration of  $1 \times 10^6$  cell per mL in culture medium. 100  $\mu$ L aliquots of cells were placed in the wells of a white-walled, white-bottomed 96-well plate (Corning, Inc. Corning, NY). 1.0  $\mu$ L of an IRM compound from Table 1 (prepared at 1 mM in 100% DMSO) was added to some cell aliquots so that the final concentration of IRM compound was 10  $\mu$ M. As a positive control, some cell aliquots were incubated with Sendai virus instead of IRM compound. As a negative control, some cell aliquots were incubated with DMSO without IRM compound. In all cases, the cells were incubated for 18 hours.

15

**Table 1 - IRM Compounds**

Compound	Chemical Name	Citation
IRM 1	4-amino-2-ethoxymethyl- $\alpha,\alpha$ -dimethyl-6,7,8,9-tetrahydro-1 <i>H</i> -imidazo[4,5- <i>c</i> ]quinoline-1-ethanol	U.S. 5,352,784 Example 91
IRM 2	4-amino- $\alpha,\alpha,2$ -trimethyl-1 <i>H</i> -imidazo[4,5- <i>c</i> ]quinoline-1-ethanol	U.S. 5,266,575 Example C1
IRM 3	N-[4-(4-amino-2-butyl-1 <i>H</i> -imidazo[4,5- <i>c</i> ]quinolin-1-yl)butyl]methanesulfonamide	U.S. 6,331,539 Example 6
IRM 4	1-{2-[3-(3-pyridyl)propoxy]ethyl}-1 <i>H</i> -imidazo[4,5- <i>c</i> ]quinolin-4-amine	WO 02/46193 Example 33
IRM 5	2-butyl-1-(2-methylpropyl)-1 <i>H</i> -imidazo[4,5- <i>c</i> ][1,5]naphthyridin-4-amine	U.S. 6,194,425 Example 39
IRM 6	2-butyl-6,7,8,9-tetrahydro-1-(2-methylpropyl)-1 <i>H</i> -imidazo[4,5- <i>c</i> ][1,5]naphthyridin-4-amine	U.S. 6,194,425 Example 40
IRM 7	N <sup>3</sup> -{4-[4-amino-2-(2-methoxyethyl)-1 <i>H</i> -imidazo[4,5- <i>c</i> ]quinolin-1-yl]butyl}-6-(1 <i>H</i> -1-pyrrolyl)nicotinamide	U.S. 6,451,810 Example 60
IRM 8	2-ethyl-1-[5-(methylsulfonyl)pentyl]-1 <i>H</i> -imidazo[4,5- <i>c</i> ]quinolin-4-amine	WO 02/46192 Example 13

The plates were equilibrated to room temperature before 1 volume of reconstituted LucLight Plus (Packard Instruments, Meriden, CT) was added to each aliquot of cells. Each well of the plate was read on an L JL Analyst (L JL Biosystems, Inc., Sunnyvale, CA) set with a 5 minute dark adapt. Data from a representative experiment are shown in Table 5 2. The data are expressed as the fold increase in luciferase induction off of the IFN- $\alpha$ 1 promoter in cell aliquots incubated with the indicated stimulant compared to the negative control in which the cell aliquots were incubated with only DMSO.

10 **Table 2 - TLR Expression by pIFN- $\alpha$ 1-luc/pCI-TLR6 Co-Transfected Namalwa cells**

<u>Stimulant</u>	<u>Fold Increase in Luciferase Induction</u>
IRM1	3.6
IRM2	2.7
IRM3	2.6
IRM4	4.0
IRM5	3.2
IRM6	2.9
IRM7	3.2
IRM8	2.3
Sendai virus	2.7

15 The complete disclosures of the patents, patent documents and publications cited herein are incorporated by reference in their entirety as if each were individually incorporated. In case of conflict, the present specification, including definitions, shall control.

20 Various modifications and alterations to this invention will become apparent to those skilled in the art without departing from the scope and spirit of this invention. Illustrative embodiments and examples are provided as examples only and are not intended to limit the scope of the present invention. The scope of the invention is limited only by the claims set forth as follows.

What is Claimed is:

1. An expression system comprising:
  - a first nucleic acid sequence that encodes a Toll-like receptor operably linked to a first expression control sequence; and
  - 5 a second nucleic acid sequence that encodes a reporter that (a) generates a detectable signal when the reporter is expressed and the cell is exposed to conditions effective for generating the detectable signal, and (b) is operably linked to a second expression control sequence that comprises a cytokine promoter, a chemokine promoter, a co-stimulatory marker promoter, or a defensin promoter.
- 10 2. The expression system of claim 1 wherein the second expression control sequence comprises an IFN- $\alpha$  promoter.
3. The expression system of claim 1 wherein the first nucleic acid sequence  
15 comprises the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, or a degenerate variant of any of the foregoing.
4. The expression system of claim 1 wherein the first nucleic acid sequence  
20 comprises a nucleotide sequence that encodes a polypeptide having the sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, or any one of the foregoing sequences with one or more conservative amino acid substitutions.
- 25 5. The expression system of claim 1 wherein the detectable signal comprises luciferase activity or  $\beta$ -galactosidase activity.
6. The expression system of claim 1 wherein a first vector comprises the first nucleic acid sequence and a second vector comprises the second nucleic acid sequence.  
30
7. A vector comprising the expression system of claim 1.

8. A TLR agonist identified using the expression system of claim 1.
9. A pharmaceutical composition comprising the TLR agonist of claim 8, or a pharmaceutically acceptable salt thereof.  
5
10. A cultured cell comprising the expression system of claim 1.
11. The cultured cell of claim 10 wherein the cell is a mammalian cell or a descendent of a mammalian cell.  
10
12. The culture cell of claim 11 wherein the cell is a human cell or a descendent of a human cell.
13. The cultured cell of claim 10 further comprising an expressible nucleic acid sequence that encodes IFN- $\alpha$  operably linked to a third expression control sequence.  
15
14. The cultured cell of claim 13 wherein the expressible nucleic acid sequence that encodes IFN- $\alpha$  is located on a chromosome of the cultured cell.
- 20 15. The cultured cell of claim 14 wherein the cultured cell is a Namalwa cell.
16. The cultured cell of claim 13 wherein the expressible nucleic acid sequence that encodes IFN- $\alpha$  is located on an extrachromosomal vector.
- 25 17. A TLR agonist identified using the cultured cell of claim 10.
18. A pharmaceutical composition comprising the TLR agonist of claim 17, or a pharmaceutically acceptable salt thereof.

30

58182US002.ST25.txt  
SEQUENCE LISTING

<110> Gupta, Shalley K.  
Ghosh, Tarun K.  
Fink, Jason R.

<120> Gene Expression Systems and Recombinant Cell Lines

<130> 58182W0003

<160> 23

<170> PatentIn version 3.1

<210> 1

<211> 2832

<212> DNA

<213> Homo sapiens

<400> 1  
acagactgcc aaatggaaca gacaaggcagg ttgtcttgt ttaaagaaaa tgagatatga 60  
gtcagttact cccggaggca atgctgctgt tcagcttgc tgtttttgt gccagggtct 120  
tcatgaacac taataggggt accaggccct cttccttgtt agaagaaatc aggataacaa 180  
aggatatattg ggcaccccta caaaaggaat ctgtatctgt atcaagatga tctgaagaac 240  
agcttctacc tttaggaatg tctagtgttc caaaatgact agcatcttcc atttgccat 300  
tatcttcatg ttaatacttc agatcagaat acaattatct gaagaaagtg aatttttagt 360  
tgataggtca aaaaacggtc tcatccacgt tcctaaagac ctatcccaga aaacaacaat 420  
cttaaatata tcgcaaaatt atatatctga gctttggact tctgacatct tatcactgtc 480  
aaaactgagg atttgataa tttctcataa tagaattccag tatcttgata tcagtgttt 540  
caaattcaac caggaattgg aatacttgaa tttgtccac aacaagttgg tgaagatttc 600  
ttgccacccct actgtgaacc tcaagcactt ggacctgtca tttaatgcat ttgatgccct 660  
gcctatatgc aaagagtttgc acaatatgtc tcaactaaaa tttctgggt tgagcaccac 720  
acacttagaa aaatcttagtgc tgctgccaat tgctcatttgc aatatcagca aggtcttgct 780  
ggtcttagga gagactttagt gggaaaaaga agaccctgag ggccttcaag actttaacac 840  
tgagagtctg cacatttgtt tccccacaaa caaagaattc cattttattt tggatgtgtc 900  
agtcaagact gtagcaaatc tggaaactatc taatatcaaa tgtgtgttag aagataacaa 960  
atgttcttac ttccctaaatgtt ttctggcgaa acttcaaaca aatccaaatgt tatcaagtct 1020  
taccttaaac aacatgaaa caacttgaa ttctttcatt aggtcctcc agctggtttgc 1080  
gcataacaact gtatggtatt tctcaatttc aaacgtgaag ctacagggtc agctggactt 1140  
cagagatttt gattattctg gcacttcctt gaaggccttgc tctatacacc aagttgtcag 1200  
cgatgtgttc ggtttccgc aaagttatcat tcatgaaatc ttttgcata tgaacatcaa 1260  
aaatttcaca gtgtctggta cacgcacgggtt ccacatgtt tgcccatcca aaatttagccc 1320

## 58182us002.ST25.txt

gttcctgcat	ttggatTTTT	ccaataatct	cttaacagac	acggTTTTG	aaaattgtgg	1380
gcaccttact	gagtggaga	cacttatttt	acaaatgaat	caattaaaag	aactttcaaa	1440
aatagctgaa	atgactcac	agatgaagtc	tctgcaacaa	ttggatatta	gccagaattc	1500
tgtaagctat	gatgaaaaga	aaggagactg	ttcttgact	aaaagtttat	taagttaaa	1560
tatgtcttca	aatatactta	ctgacactat	tttcagatgt	ttacctccca	ggatcaaggt	1620
acttgatctt	cacagcaata	aaataaagag	cattcctaaa	caagtcgtaa	aactggaaGC	1680
tttgcaagaa	ctcaatgttg	ctttcaattc	tttaactgac	cttcctggat	gtggcagctt	1740
tagcagcctt	tctgtattga	tcattgatca	caattcagtt	tcccacccat	cagctgattt	1800
cttccagagc	tgccagaaga	tgaggtcaat	aaaagcaggg	gacaatccat	tccaatgtac	1860
ctgtgagcta	ggagaatttG	tcaaaaatAT	agaccaagta	tcaagtgaag	tgttagaggg	1920
ctggcctgat	tcttataagt	gtgactacCC	ggaaagtTAT	agaggaACCC	tactaaagga	1980
ctttcacatg	tctgaatttA	cctgcaacat	aactctgCTG	atcgTCacca	tcgttGCCAC	2040
catgctggtg	ttggctgtGA	ctgtgacCTC	cctctgcatc	tacttggatc	tgccctggta	2100
tctcaggatg	gtgtGCCAGT	ggacCCAGAC	ccggcgcagg	gccaggaaca	tacccttaga	2160
agaactccaa	agaaatctcc	agtttcatgc	atttatttca	tatagtggc	acgattctt	2220
ctgggtgaag	aatgaatttA	tgccaaacct	agagaaagaa	ggtatgcaga	tttgccttca	2280
tgagagaaac	tttgtccTG	gcaagagcat	tgtggaaat	atcatcacct	gcattgagaa	2340
gagttacaag	tccatTTTg	tttgtctcc	caactttgtc	cagagtgaat	ggtgccattA	2400
tgaactctac	tttgcCcATC	acaatctctt	tcatgaagga	tctaataGCT	taatcctgat	2460
cttgctggaa	cccattCCGc	agtactccat	tccttagcagt	tatcacaAGC	tcaaaagtct	2520
catggccagg	aggacttatt	tggaatggcc	caagggaaAG	agcaaACGTG	gcctttttG	2580
ggctaactta	agggcagCCA	ttaatattaa	gctgacagag	caagcaaAGA	aatagattac	2640
acatcaagtG	aaaaatattc	ctcctgttGA	tattgtctG	tttggaaagtT	ccaacaatga	2700
ctttatTTG	catcagcata	gatgtaaACA	caattgtgag	tgtatgtatgt	aggtaaaaat	2760
atataccTTc	gggtcgcagt	tcaccatttA	tatgtgttat	taaaaattaa	tgaaatgata	2820
taactttgat	tt					2832

<210> 2  
<211> 786  
<212> PRT  
<213> Homo sapiens

<400> 2

Met Thr Ser Ile Phe His Phe Ala Ile Ile Phe Met Leu Ile Leu Gln  
1 5 10 15

## 58182US002.ST25.txt

Ile Arg Ile Gln Leu Ser Glu Glu Ser Glu Phe Leu Val Asp Arg Ser  
20 25 30

Lys Asn Gly Leu Ile His Val Pro Lys Asp Leu Ser Gln Lys Thr Thr  
35 40 45

Ile Leu Asn Ile Ser Gln Asn Tyr Ile Ser Glu Leu Trp Thr Ser Asp  
50 55 60

Ile Leu Ser Leu Ser Lys Leu Arg Ile Leu Ile Ile Ser His Asn Arg  
65 70 75 80

Ile Gln Tyr Leu Asp Ile Ser Val Phe Lys Phe Asn Gln Glu Leu Glu  
85 90 95

Tyr Leu Asp Leu Ser His Asn Lys Leu Val Lys Ile Ser Cys His Pro  
100 105 110

Thr Val Asn Leu Lys His Leu Asp Leu Ser Phe Asn Ala Phe Asp Ala  
115 120 125

Leu Pro Ile Cys Lys Glu Phe Gly Asn Met Ser Gln Leu Lys Phe Leu  
130 135 140

Gly Leu Ser Thr Thr His Leu Glu Lys Ser Ser Val Leu Pro Ile Ala  
145 150 155 160

His Leu Asn Ile Ser Lys Val Leu Leu Val Leu Gly Glu Thr Tyr Gly  
165 170 175

Glu Lys Glu Asp Pro Glu Gly Leu Gln Asp Phe Asn Thr Glu Ser Leu  
180 185 190

His Ile Val Phe Pro Thr Asn Lys Glu Phe His Phe Ile Leu Asp Val  
195 200 205

Ser Val Lys Thr Val Ala Asn Leu Glu Leu Ser Asn Ile Lys Cys Val  
210 215 220

Leu Glu Asp Asn Lys Cys Ser Tyr Phe Leu Ser Ile Leu Ala Lys Leu  
225 230 235 240

Gln Thr Asn Pro Lys Leu Ser Ser Leu Thr Leu Asn Asn Ile Glu Thr  
245 250 255

Thr Trp Asn Ser Phe Ile Arg Ile Leu Gln Leu Val Trp His Thr Thr  
Page 3

58182US002.ST25.txt  
260                    265                    270

Val Trp Tyr Phe Ser Ile Ser Asn Val Lys Leu Gln Gly Gln Leu Asp  
275                    280                    285

Phe Arg Asp Phe Asp Tyr Ser Gly Thr Ser Leu Lys Ala Leu Ser Ile  
290                    295                    300

His Gln Val Val Ser Asp Val Phe Gly Phe Pro Gln Ser Tyr Ile Tyr  
305                    310                    315                    320

Glu Ile Phe Ser Asn Met Asn Ile Lys Asn Phe Thr Val Ser Gly Thr  
325                    330                    335

Arg Met Val His Met Leu Cys Pro Ser Lys Ile Ser Pro Phe Leu His  
340                    345                    350

Leu Asp Phe Ser Asn Asn Leu Leu Thr Asp Thr Val Phe Glu Asn Cys  
355                    360                    365

Gly His Leu Thr Glu Leu Glu Thr Leu Ile Leu Gln Met Asn Gln Leu  
370                    375                    380

Lys Glu Leu Ser Lys Ile Ala Glu Met Thr Thr Gln Met Lys Ser Leu  
385                    390                    395                    400

Gln Gln Leu Asp Ile Ser Gln Asn Ser Val Ser Tyr Asp Glu Lys Lys  
405                    410                    415

Gly Asp Cys Ser Trp Thr Lys Ser Leu Leu Ser Leu Asn Met Ser Ser  
420                    425                    430

Asn Ile Leu Thr Asp Thr Ile Phe Arg Cys Leu Pro Pro Arg Ile Lys  
435                    440                    445

Val Leu Asp Leu His Ser Asn Lys Ile Lys Ser Ile Pro Lys Gln Val  
450                    455                    460

Val Lys Leu Glu Ala Leu Gln Glu Leu Asn Val Ala Phe Asn Ser Leu  
465                    470                    475                    480

Thr Asp Leu Pro Gly Cys Gly Ser Phe Ser Ser Leu Ser Val Leu Ile  
485                    490                    495

Ile Asp His Asn Ser Val Ser His Pro Ser Ala Asp Phe Phe Gln Ser  
500                    505                    510

58182US002.ST25.txt

Cys Gln Lys Met Arg Ser Ile Lys Ala Gly Asp Asn Pro Phe Gln Cys  
515 520 525

Thr Cys Glu Leu Gly Glu Phe Val Lys Asn Ile Asp Gln Val Ser Ser  
530 535 540

Glu Val Leu Glu Gly Trp Pro Asp Ser Tyr Lys Cys Asp Tyr Pro Glu  
545 550 555 560

Ser Tyr Arg Gly Thr Leu Leu Lys Asp Phe His Met Ser Glu Leu Ser  
565 570 575

cys Asn Ile Thr Leu Leu Ile Val Thr Ile Val Ala Thr Met Leu Val  
580 585 590

Leu Ala Val Thr Val Thr Ser Leu Cys Ile Tyr Leu Asp Leu Pro Trp  
595 600 605

Tyr Leu Arg Met Val Cys Gln Trp Thr Gln Thr Arg Arg Arg Ala Arg  
610 615 620

Asn Ile Pro Leu Glu Glu Leu Gln Arg Asn Leu Gln Phe His Ala Phe  
625 630 635 640

Ile Ser Tyr Ser Gly His Asp Ser Phe Trp Val Lys Asn Glu Leu Leu  
645 650 655

Pro Asn Leu Glu Lys Glu Gly Met Gln Ile Cys Leu His Glu Arg Asn  
660 665 670

Phe Val Pro Gly Lys Ser Ile Val Glu Asn Ile Ile Thr Cys Ile Glu  
675 680 685

Lys Ser Tyr Lys Ser Ile Phe Val Leu Ser Pro Asn Phe Val Gln Ser  
690 695 700

Glu Trp Cys His Tyr Glu Leu Tyr Phe Ala His His Asn Leu Phe His  
705 710 715 720

Glu Gly Ser Asn Ser Leu Ile Leu Ile Leu Glu Pro Ile Pro Gln  
725 730 735

Tyr Ser Ile Pro Ser Ser Tyr His Lys Leu Lys Ser Leu Met Ala Arg  
740 745 750

Arg Thr Tyr Leu Glu Trp Pro Lys Glu Lys Ser Lys Arg Gly Leu Phe  
755 760 765

## 58182US002.ST25.txt

Trp Ala Asn Leu Arg Ala Ala Ile Asn Ile Lys Leu Thr Glu Gln Ala  
 770                           775                           780

Lys Lys  
 785

<210>	3					
<211>	2621					
<212>	DNA					
<213>	Homo sapiens					
<400>	3					
cagtgtttgg	tgttgcaagc	aggatccaaa	ggagacctat	agtgactccc	aggagcttt	60
agtgaccaag	tgaaggtaacc	tgtggggctc	atttgtcccc	ttgtcttttc	actgctttca	120
actggtagtt	gtgggttcaa	gcactggaca	atgccacata	ctttgtggat	ggtgtgggtc	180
ttgggggtca	tcatcagcct	ctccaaggaa	gaatccctcca	atcaggcttc	tctgtcttgt	240
gaccgcaatg	gtatctgcaa	gggcagctca	ggatcttaa	actccattcc	ctcagggctc	300
acagaagctg	taaaaagcct	tgacctgtcc	aacaacagga	tcacacctat	tagcaacagt	360
gacctacaga	ggtgtgtcaa	cctccaggct	ctgggtctga	cattcaatgg	aattaacaca	420
atagaggaag	attcttttc	ttccctgggc	agtcttgaac	atttagactt	atcctataat	480
tacttatcta	atttatcgtc	ttcctggttc	aagccccctt	cttcttaac	attcttaaac	540
ttactggaa	atccttacaa	aaccctaggg	gaaacatctc	tttttctca	tctcacaaaa	600
ttgcaaatcc	tgagagtggg	aaatatggac	acttcacta	agattcaaag	aaaagatttt	660
gctggactta	cctcccttga	ggaacttgag	attgatgctt	cagatctaca	gagctatgag	720
ccaaaaagtt	tgaagtcaat	tcagaatgt	agtcatctga	tccttcatat	gaagcagcat	780
attttactgc	tggagatttt	tgttagatgtt	acaagttccg	tggatgttt	ggaactgcga	840
gatactgatt	tggacacttt	ccattttca	gaactatcca	ctggtaaac	aaattcattg	900
attaaaaagt	ttacatttag	aaatgtgaaa	atcaccgatg	aaagtttgg	tcaggttatg	960
aaactttga	atcagatttc	tggattgtta	gaatttagagt	ttgatgactg	tacccttaat	1020
ggagttggta	attttagagc	atctgataat	gacagagtt	tagatccagg	taaagtggaa	1080
acgttaacaa	tccggaggct	gcatattcca	aggtttact	tatttatga	tctgagcact	1140
ttatattcac	ttacagaaaag	agttaaaaga	atcacagtag	aaaacagtaa	agttttctg	1200
gttccttgg	tactttcaca	acatttaaaa	tcattagaat	acttggatct	cagtaaaaat	1260
ttgatggttg	aagaatactt	aaaaaattca	gcctgtgagg	atgcctggcc	ctctctacaa	1320
actttaattt	taaggcaaaa	tcatttggca	tcattggaaa	aaaccggaga	gactttgctc	1380
actctgaaaa	acttgactaa	cattgatatac	agtaagaata	gtttcattc	tatgcctgaa	1440

58182US002.ST25.txt

acttgtcagt ggccagaaaa gatgaaatat ttgaacttat ccagcacacg aatacacagt	1500
gtaacaggct gcattccaa gacactggaa atttttagatg ttagcaacaa caatctcaat	1560
ttatttctt tgaatttgc gcaactcaa gaaccttata ttccagaaa taagttgtat	1620
actctaccag atgcctccct cttacccatg ttacttagtat tgaaaatcag taggaatgca	1680
ataactacgt tttctaagga gcaacttgac tcatttcaca cactgaagac tttggaagct	1740
ggtggcaata acttcatttgc tcctgtgaa ttccctccct tcactcagga gcagcaagca	1800
ctggccaaag tcttgattga ttggccagca aattacctgt gtgactctcc atcccatgtg	1860
cgtggccagc aggttcagga tgtccgcctc tcgggtgtcg aatgtcacag gacagcactg	1920
gtgtctggca tgtgctgtgc tctgttcctg ctgatcctgc tcacgggggt cctgtgccac	1980
cgtttccatg gcctgtggta tatgaaaatg atgtggcct ggctccaggc caaaaggaag	2040
cccaggaaag ctcccagcag gaacatctgc tatgtatgc ttgttctta cagtgagcgg	2100
gatgcctact gggtgagaa ccttatggtc caggagctgg agaacttcaa tcccccttc	2160
aagttgtgtc ttcataagcg ggacttcatt cctggcaagt ggatcattga caatatcatt	2220
gactccattt gaaagagcca caaaactgtc tttgtcttt ctgaaaactt tgtgaagagt	2280
gagtggtgca agtatgaact ggacttctcc catttcgtc ttttgatga gaacaatgat	2340
gctgccattc tcatttcttgc ggagcccatt gagaaaaaaag ccattccccca gcgcttctgc	2400
aagctgcgga agataatgaa caccaagacc tacctggagt ggcccatgga cgaggctcag	2460
cggaaaggat tttggtaaa tctgagagct gcgataaaagt cctaggttcc cataatttaag	2520
accagtctt gtctagttgg gatctttatg tcacttagtt tagttaaatg cattcagaca	2580
taattatata aaaactacgt ggatgtaccg tcatttgagg a	2621

<210> 4  
<211> 784  
<212> PRT

<213> Homo sapiens

<400> 4

Met Pro His Thr Leu Trp Met Val Trp Val Leu Gly Val Ile Ile Ser  
1               5               10               15

Leu Ser Lys Glu Glu Ser Ser Asn Gln Ala Ser Leu Ser Cys Asp Arg  
20               25               30

Asn Gly Ile Cys Lys Gly Ser Ser Gly Ser Leu Asn Ser Ile Pro Ser  
35               40               45

Gly Leu Thr Glu Ala Val Lys Ser Leu Asp Leu Ser Asn Asn Arg Ile  
50               55               60

## 58182US002.ST25.txt

Thr Tyr Ile Ser Asn Ser Asp Leu Gln Arg Cys Val Asn Leu Gln Ala  
65 70 75 80

Leu Val Leu Thr Ser Asn Gly Ile Asn Thr Ile Glu Glu Asp Ser Phe  
85 90 95

Ser Ser Leu Gly Ser Leu Glu His Leu Asp Leu Ser Tyr Asn Tyr Leu  
100 105 110

Ser Asn Leu Ser Ser Ser Trp Phe Lys Pro Leu Ser Ser Leu Thr Phe  
115 120 125

Leu Asn Leu Leu Gly Asn Pro Tyr Lys Thr Leu Gly Glu Thr Ser Leu  
130 135 140

Phe Ser His Leu Thr Lys Leu Gln Ile Leu Arg Val Gly Asn Met Asp  
145 150 155 160

Thr Phe Thr Lys Ile Gln Arg Lys Asp Phe Ala Gly Leu Thr Phe Leu  
165 170 175

Glu Glu Leu Glu Ile Asp Ala Ser Asp Leu Gln Ser Tyr Glu Pro Lys  
180 185 190

Ser Leu Lys Ser Ile Gln Asn Val Ser His Leu Ile Leu His Met Lys  
195 200 205

Gln His Ile Leu Leu Leu Glu Ile Phe Val Asp Val Thr Ser Ser Val  
210 215 220

Glu Cys Leu Glu Leu Arg Asp Thr Asp Leu Asp Thr Phe His Phe Ser  
225 230 235 240

Glu Leu Ser Thr Gly Glu Thr Asn Ser Leu Ile Lys Lys Phe Thr Phe  
245 250 255

Arg Asn Val Lys Ile Thr Asp Glu Ser Leu Phe Gln Val Met Lys Leu  
260 265 270

Leu Asn Gln Ile Ser Gly Leu Leu Glu Leu Glu Phe Asp Asp Cys Thr  
275 280 285

Leu Asn Gly Val Gly Asn Phe Arg Ala Ser Asp Asn Asp Arg Val Ile  
290 295 300

Asp Pro Gly Lys Val Glu Thr Leu Thr Ile Arg Arg Leu His Ile Pro  
305 310 315 320

## 58182US002.ST25.txt

Arg Phe Tyr Leu Phe Tyr Asp Leu Ser Thr Leu Tyr Ser Leu Thr Glu  
325 330 335

Arg Val Lys Arg Ile Thr Val Glu Asn Ser Lys Val Phe Leu Val Pro  
340 345 350

Cys Leu Leu Ser Gln His Leu Lys Ser Leu Glu Tyr Leu Asp Leu Ser  
355 360 365

Glu Asn Leu Met Val Glu Glu Tyr Leu Lys Asn Ser Ala Cys Glu Asp  
370 375 380

Ala Trp Pro Ser Leu Gln Thr Leu Ile Leu Arg Gln Asn His Leu Ala  
385 390 395 400

Ser Leu Glu Lys Thr Gly Glu Thr Leu Leu Thr Leu Lys Asn Leu Thr  
405 410 415

Asn Ile Asp Ile Ser Lys Asn Ser Phe His Ser Met Pro Glu Thr Cys  
420 425 430

Gln Trp Pro Glu Lys Met Lys Tyr Leu Asn Leu Ser Ser Thr Arg Ile  
435 440 445

His Ser Val Thr Gly Cys Ile Pro Lys Thr Leu Glu Ile Leu Asp Val  
450 455 460

Ser Asn Asn Asn Leu Asn Leu Phe Ser Leu Asn Leu Pro Gln Leu Lys  
465 470 475 480

Glu Leu Tyr Ile Ser Arg Asn Lys Leu Met Thr Leu Pro Asp Ala Ser  
485 490 495

Leu Leu Pro Met Leu Leu Val Leu Lys Ile Ser Arg Asn Ala Ile Thr  
500 505 510

Thr Phe Ser Lys Glu Gln Leu Asp Ser Phe His Thr Leu Lys Thr Leu  
515 520 525

Glu Ala Gly Gly Asn Asn Phe Ile Cys Ser Cys Glu Phe Leu Ser Phe  
530 535 540

Thr Gln Glu Gln Gln Ala Leu Ala Lys Val Leu Ile Asp Trp Pro Ala  
545 550 555 560

Asn Tyr Leu Cys Asp Ser Pro Ser His Val Arg Gly Gln Gln Val Gln

## 58182US002.ST25.txt

565

570

575

Asp Val Arg Leu Ser Val Ser Glu Cys His Arg Thr Ala Leu Val Ser  
 580 585 590

Gly Met Cys Cys Ala Leu Phe Leu Leu Ile Leu Leu Thr Gly Val Leu  
 595 600 605

Cys His Arg Phe His Gly Leu Trp Tyr Met Lys Met Met Trp Ala Trp  
 610 615 620

Leu Gln Ala Lys Arg Lys Pro Arg Lys Ala Pro Ser Arg Asn Ile Cys  
 625 630 635 640

Tyr Asp Ala Phe Val Ser Tyr Ser Glu Arg Asp Ala Tyr Trp Val Glu  
 645 650 655

Asn Leu Met Val Gln Glu Leu Glu Asn Phe Asn Pro Pro Phe Lys Leu  
 660 665 670

Cys Leu His Lys Arg Asp Phe Ile Pro Gly Lys Trp Ile Ile Asp Asn  
 675 680 685

Ile Ile Asp Ser Ile Glu Lys Ser His Lys Thr Val Phe Val Leu Ser  
 690 695 700

Glu Asn Phe Val Lys Ser Glu Trp Cys Lys Tyr Glu Leu Asp Phe Ser  
 705 710 715 720

His Phe Arg Leu Phe Asp Glu Asn Asn Asp Ala Ala Ile Leu Ile Leu  
 725 730 735

Leu Glu Pro Ile Glu Lys Lys Ala Ile Pro Gln Arg Phe Cys Lys Leu  
 740 745 750

Arg Lys Ile Met Asn Thr Lys Thr Tyr Leu Glu Trp Pro Met Asp Glu  
 755 760 765

Ala Gln Arg Glu Gly Phe Trp Val Asn Leu Arg Ala Ala Ile Lys Ser  
 770 775 780

&lt;210&gt; 5

&lt;211&gt; 3057

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 5

cactttcgag agtgccgtct atttgccaca cacttccctg atgaaatgtc tggatttgga

60

58182US002.ST25.txt

ctaaagaaaa aaggaaaggc tagcagtcat ccaacagaat catgagacag actttgcctt	120
gtatctactt ttgggggggc ctttgccct ttggatgct gtgtgcattc tccaccacca	180
agtcaactgt tagccatgaa gttgctgact gcagccaccc gaagttgact caggtacccg	240
atgatctacc cacaacata acagtgtga accttaccca taatcaactc agaagattac	300
cagccgcca cttcacaagg tatagccagc taacttagctt ggatgttagga tttaacacca	360
tctcaaaact ggagccagaa ttgtgccaga aacttcccat gttaaaagtt ttgaacctcc	420
agcacaatga gctatctcaa ctttctgata aaaccttgc cttctgcacg aatttgactg	480
aactccatct catgtccaaac tcaatccaga aaattaaaaa taatccctt gtcaagcaga	540
agaatttaat cacattagat ctgtctcata atggcttgtc atctacaaaa ttaggaactc	600
aggttcagct ggaaaatctc caagagcttc tattatcaa caataaaatt caagcgctaa	660
aaagtgaaga actggatatc tttgccaatt catctttaaa aaaatttagag ttgtcatcga	720
atcaaattaa agagtttct ccagggtgtt ttcacgcaat tggaaagatta tttggcctct	780
ttctgaacaa tgtccagctg ggtcccagcc ttacagagaa gctatgtttg gaatttagcaa	840
acacaagcat tcggaatctg tctctgagta acagccagct gtccaccacc agcaatacaa	900
ctttcttggg actaaagtgg acaaatctca ctatgctcga tcttcctac aacaacttaa	960
atgtggttgg taacgattcc tttgcttggc ttccacaact agaatatttc ttcctagagt	1020
ataataatat acagcatttgc ttttctcact cttgcacgg gctttcaat gtgaggtacc	1080
tgaatttgaa acggctttt actaaacaaa gtatccct tgccctactc cccaaagattg	1140
atgatttttc ttttcagtgg ctaaaatgtt tggagcacct taacatggaa gataatgata	1200
ttccaggcat aaaaagcaat atgttcacag gattgataaa cctgaaatac ttaagtctat	1260
ccaaactcctt tacaagtttgc cgaactttga caaatgaaac atttgttatca cttgctcatt	1320
ctccccttaca catactcaac ctaaccaaga ataaaatctc aaaaatagag agtgatgctt	1380
tctcttgggtt gggccaccta gaagtacttg acctggcct taatgaaatt gggcaagaac	1440
tcacaggcca ggaatggaga ggtctagaaa atatttcga aatctatctt tcctacaaca	1500
agtacctgca gctgactagg aactcccttg cttggccc aagccttcaa cgactgatgc	1560
tccgaagggtt ggccttaaa aatgtggata gctctccctc accattccag cctcttcgtt	1620
acttgaccat tctggatcta agcaacaaca acatagccaa cataaatgat gacatgttgg	1680
agggtcttgc gaaactagaa attctcgatt tgcagcataa caacttagca cggctctgg	1740
aacacgcaaa ccctgggtt cccatatttatt tcctaaaggg tctgtctcac ctccacatcc	1800
ttaacttggc gtccaaacggc tttgacgaga tcccagttga ggtcttcaag gatttatttg	1860
aactaaagat catcgatttgc ggattgaata atttaaacac acttccagca tctgtcttta	1920
ataatcagggt gtctctaaag tcattgaacc ttcagaagaa tctcataaca tccgttgg	1980

## 58182US002.ST25.txt

agaaggttt cgggccagct ttcaggaacc tgactgagtt agatatgcgc ttaatccct	2040
ttgattgcac gtgtgaaagt attgcctggc ttgttaattt gattaacgag acccatacca	2100
acatccctga gctgtcaagc cactacccccc gcaacactcc acctcactat catgggttcc	2160
cagttagact ttttgataca tcatacttgca aagacagtgc ccccttgaa ctcttttca	2220
tgtatcaatac cagtatccctg ttgatTTTta tctttattgt acttctcatc cactttgagg	2280
gctggaggat atcttttat tggaaatgtt cagtacatcg agttcttggc ttcaaagaaa	2340
tagacagaca gacagaacag tttgaatatg cagcatatat aattcatgcc tataaagata	2400
aggattgggt ctgggaacat ttctcttcaa tggaaaagga agaccaatct ctcaaatttt	2460
gtcttggaga aagggacttt gaggcgggtg ttttgaact agaagcaatt gttaacagca	2520
tcaaaaagaag cagaaaaattt atttttgtt taacacacca tctattaaaa gaccattat	2580
gcaaaagatt caaggtacat catgcagttc aacaagctat tgaacaaaat ctggattcca	2640
ttatatttgtt ttcccttgag gagattccag attataactt gaaccatgca ctctgttgc	2700
gaagaggaat gtttaaatct cactgcacat tgaactggcc agttcagaaa gaacggatag	2760
gtgccttcg tcataaattt cagtagcac ttggatccaa aaactctgtt cattaaattt	2820
atttaaat tcaatttagca aaggagaaac tttctcaatt taaaaagttc tatggcaaatt	2880
ttaagtttc cataaagggtt ttataattttt tttattcata tttgtaaatg attatattct	2940
atcacaattt catctttctt agggaaatgt gtctccttattt ttcaggccta ttttgacaa	3000
ttgacttaat tttacccaaa ataaaacata taagcacgtt aaaaaaaaaa aaaaaaaaaa	3057

<210> 6  
 <211> 904  
 <212> PRT  
 <213> Homo sapiens  
 <400> 6

Met Arg Gln Thr Leu Pro Cys Ile Tyr Phe Trp Gly Gly Leu Leu Pro  
 1 5 10 15

Phe Gly Met Leu Cys Ala Ser Ser Thr Thr Lys Cys Thr Val Ser His  
 20 25 30

Glu Val Ala Asp Cys Ser His Leu Lys Leu Thr Gln Val Pro Asp Asp  
 35 40 45

Leu Pro Thr Asn Ile Thr Val Leu Asn Leu Thr His Asn Gln Leu Arg  
 50 55 60

Arg Leu Pro Ala Ala Asn Phe Thr Arg Tyr Ser Gln Leu Thr Ser Leu  
 65 70 75 80

## 58182US002.ST25.txt

Asp Val Gly Phe Asn Thr Ile Ser Lys Leu Glu Pro Glu Leu Cys Gln  
85 90 95

Lys Leu Pro Met Leu Lys Val Leu Asn Leu Gln His Asn Glu Leu Ser  
100 105 110

Gln Leu Ser Asp Lys Thr Phe Ala Phe Cys Thr Asn Leu Thr Glu Leu  
115 120 125

His Leu Met Ser Asn Ser Ile Gln Lys Ile Lys Asn Asn Pro Phe Val  
130 135 140

Lys Gln Lys Asn Leu Ile Thr Leu Asp Leu Ser His Asn Gly Leu Ser  
145 150 155 160

Ser Thr Lys Leu Gly Thr Gln Val Gln Leu Glu Asn Leu Gln Glu Leu  
165 170 175

Leu Leu Ser Asn Asn Lys Ile Gln Ala Leu Lys Ser Glu Glu Leu Asp  
180 185 190

Ile Phe Ala Asn Ser Ser Leu Lys Lys Leu Glu Leu Ser Ser Asn Gln  
195 200 205

Ile Lys Glu Phe Ser Pro Gly Cys Phe His Ala Ile Gly Arg Leu Phe  
210 215 220

Gly Leu Phe Leu Asn Asn Val Gln Leu Gly Pro Ser Leu Thr Glu Lys  
225 230 235 240

Leu Cys Leu Glu Leu Ala Asn Thr Ser Ile Arg Asn Leu Ser Leu Ser  
245 250 255

Asn Ser Gln Leu Ser Thr Thr Ser Asn Thr Thr Phe Leu Gly Leu Lys  
260 265 270

Trp Thr Asn Leu Thr Met Leu Asp Leu Ser Tyr Asn Asn Leu Asn Val  
275 280 285

Val Gly Asn Asp Ser Phe Ala Trp Leu Pro Gln Leu Glu Tyr Phe Phe  
290 295 300

Leu Glu Tyr Asn Asn Ile Gln His Leu Phe Ser His Ser Leu His Gly  
305 310 315 320

Leu Phe Asn Val Arg Tyr Leu Asn Leu Lys Arg Ser Phe Thr Lys Gln

## 58182us002.ST25.txt

325

330

335

Ser Ile Ser Leu Ala Ser Leu Pro Lys Ile Asp Asp Phe Ser Phe Gln  
340 345 350

Trp Leu Lys Cys Leu Glu His Leu Asn Met Glu Asp Asn Asp Ile Pro  
355 360 365

Gly Ile Lys Ser Asn Met Phe Thr Gly Leu Ile Asn Leu Lys Tyr Leu  
370 375 380

Ser Leu Ser Asn Ser Phe Thr Ser Leu Arg Thr Leu Thr Asn Glu Thr  
385 390 395 400

Phe Val Ser Leu Ala His Ser Pro Leu His Ile Leu Asn Leu Thr Lys  
405 410 415

Asn Lys Ile Ser Lys Ile Glu Ser Asp Ala Phe Ser Trp Leu Gly His  
420 425 430

Leu Glu Val Leu Asp Leu Gly Leu Asn Glu Ile Gly Gln Glu Leu Thr  
435 440 445

Gly Gln Glu Trp Arg Gly Leu Glu Asn Ile Phe Glu Ile Tyr Leu Ser  
450 455 460

Tyr Asn Lys Tyr Leu Gln Leu Thr Arg Asn Ser Phe Ala Leu Val Pro  
465 470 475 480

Ser Leu Gln Arg Leu Met Leu Arg Arg Val Ala Leu Lys Asn Val Asp  
485 490 495

Ser Ser Pro Ser Pro Phe Gln Pro Leu Arg Asn Leu Thr Ile Leu Asp  
500 505 510

Leu Ser Asn Asn Asn Ile Ala Asn Ile Asn Asp Asp Met Leu Glu Gly  
515 520 525

Leu Glu Lys Leu Glu Ile Leu Asp Leu Gln His Asn Asn Leu Ala Arg  
530 535 540

Leu Trp Lys His Ala Asn Pro Gly Gly Pro Ile Tyr Phe Leu Lys Gly  
545 550 555 560

Leu Ser His Leu His Ile Leu Asn Leu Glu Ser Asn Gly Phe Asp Glu  
565 570 575

58182US002.ST25.txt

Ile Pro Val Glu Val Phe Lys Asp Leu Phe Glu Leu Lys Ile Ile Asp  
580 585 590

Leu Gly Leu Asn Asn Leu Asn Thr Leu Pro Ala Ser Val Phe Asn Asn  
595 600 605

Gln Val Ser Leu Lys Ser Leu Asn Leu Gln Lys Asn Leu Ile Thr Ser  
610 615 620

Val Glu Lys Lys Val Phe Gly Pro Ala Phe Arg Asn Leu Thr Glu Leu  
625 630 635 640

Asp Met Arg Phe Asn Pro Phe Asp Cys Thr Cys Glu Ser Ile Ala Trp  
645 650 655

Phe Val Asn Trp Ile Asn Glu Thr His Thr Asn Ile Pro Glu Leu Ser  
660 665 670

Ser His Tyr Leu Cys Asn Thr Pro Pro His Tyr His Gly Phe Pro Val  
675 680 685

Arg Leu Phe Asp Thr Ser Ser Cys Lys Asp Ser Ala Pro Phe Glu Leu  
690 695 700

Phe Phe Met Ile Asn Thr Ser Ile Leu Leu Ile Phe Ile Phe Ile Val  
705 710 715 720

Leu Leu Ile His Phe Glu Gly Trp Arg Ile Ser Phe Tyr Trp Asn Val  
725 730 735

Ser Val His Arg Val Leu Gly Phe Lys Glu Ile Asp Arg Gln Thr Glu  
740 745 750

Gln Phe Glu Tyr Ala Ala Tyr Ile Ile His Ala Tyr Lys Asp Lys Asp  
755 760 765

Trp Val Trp Glu His Phe Ser Ser Met Glu Lys Glu Asp Gln Ser Leu  
770 775 780

Lys Phe Cys Leu Glu Glu Arg Asp Phe Glu Ala Gly Val Phe Glu Leu  
785 790 795 800

Glu Ala Ile Val Asn Ser Ile Lys Arg Ser Arg Lys Ile Ile Phe Val  
805 810 815

Ile Thr His His Leu Leu Lys Asp Pro Leu Cys Lys Arg Phe Lys Val  
820 825 830

## 58182US002.ST25.txt

His His Ala Val Gln Gln Ala Ile Glu Gln Asn Leu Asp Ser Ile Ile  
 835 840 845

Leu Val Phe Leu Glu Glu Ile Pro Asp Tyr Lys Leu Asn His Ala Leu  
 850 855 860

Cys Leu Arg Arg Gly Met Phe Lys Ser His Cys Ile Leu Asn Trp Pro  
 865 870 875 880

Val Gln Lys Glu Arg Ile Gly Ala Phe Arg His Lys Leu Gln Val Ala  
 885 890 895

Leu Gly Ser Lys Asn Ser Val His  
 900

<210> 7  
<211> 3811  
<212> DNA  
<213> Homo sapiens

<400> 7		
acaggccac tgctgctcac agaagcagtg aggatgatgc caggatgatg tctgcctcg	60	
gcctggctgg gactctgatc ccagccatgg cttcccttc ctgcgtgaga ccagaaagct	120	
gggagccctg cgtggagact tggccctaaa ccacacagaa gagctggcat gaaaccaga	180	
gtttcagac tccggagcct cagcccttca ccccgattcc attgcttctt gctaaatgct	240	
gccgttttat cacggaggtg gttcctaata ttacttatca atgcatggag ctgaatttct	300	
acaatccc cgacaacctc cccttctcaa ccaagaacct ggacctgagc ttatcccc	360	
tgaggcattt aggcagctat agcttcttca gtttccaga actgcaggtg ctggatttat	420	
ccaggtgtga aatccagaca attgaagatg gggcatatca gagcctaagc cacctctcta	480	
ccttaatatt gacagaaac cccatccaga gtttagccct gggagccttt tctggactat	540	
caagtttaca gaagctggtg gctgtggaga caaatctagc atctctagag aacttcccc	600	
ttggacatct caaaactttg aaagaactta atgtggctca caatcttatac caatcttca	660	
aattacctga gtattttct aatctgacca atctagagca ctggacctt tccagcaaca	720	
agattcaaag tatattattgc acagacttgc ggttctaca tcaaattgccc ctactcaatc	780	
tctctttaga cctgtccctg aaccctatga actttatcca accaggtgca tttaaagaaa	840	
ttaggcttca taagctgact ttaagaata atttgatag tttaaatgta atgaaaactt	900	
gtattcaagg tctggctggt ttagaagtcc atcggttggt tctggagaa tttagaaatg	960	
aaggaaactt ggaaaagttt gacaaatctg ctctagaggg cctgtgcaat ttgaccattg	1020	
aagaattccg attagcatac ttagactact acctcgatga tattattgac ttatctaatt	1080	

58182US002.ST25.txt

gtttgacaaa	tgttcttca	tttccctgg	tgagtgtgac	tattgaaagg	gtaaaagact	1140
tttcttataa	tttcggatgg	caacattnag	aatttagttaa	ctgtaaattt	ggacagttc	1200
ccacattgaa	actcaaatct	ctcaaaaaggc	ttactttcac	ttccaacaaa	ggtgggaatg	1260
cttttcaga	agttgatcta	ccaagccttg	agtttctaga	tctcagtaga	aatggcttga	1320
gtttcaaagg	ttgctgttct	caaagtgatt	ttgggacaac	cagcctaaag	tattnagatc	1380
tgagcttcaa	tggtgttatt	accatgagtt	caaacttctt	gggcttagaa	caactagaac	1440
atctggattt	ccagcattcc	aatttgaac	aatgagtga	gttttcagta	ttcctatcac	1500
tcagaaacct	catttacctt	gacatttctc	atactcacac	cagagttgct	ttcaatggca	1560
tcttcaatgg	cttgcctcagt	ctcgaagtct	tgaaaatggc	tggcaattct	ttccaggaaaa	1620
acttccttcc	agatatcttc	acagagctga	gaaacttgac	cttcctggac	ctctctcagt	1680
gtcaactgga	gcagttgtct	ccaacagcat	ttaactcact	ctccagtcct	caggtactaa	1740
atatgagcca	caacaacttc	ttttcattgg	atacgtttcc	ttataagtgt	ctgaactccc	1800
tccaggttct	tgattacagt	ctcaatcaca	taatgacttc	caaaaaacag	gaactacagc	1860
attttccaag	tagtctagct	ttcttaaattc	ttactcagaa	tgactttgct	tgtacttgc	1920
aacaccagag	tttcctgcaa	tggatcaagg	accagaggca	gctcttggtg	gaagttgaac	1980
gaatggaatg	tgcaacaccc	tcagataagc	aggcatgcc	tgtgctgagt	ttgaatatca	2040
cctgtcagat	gaataagacc	atcattggtg	tgtcggtcct	cagtgtgctt	gtatgtatctg	2100
ttttagcgt	tctggcttat	aagttctatt	ttcacctgat	gcttcttgct	ggctgcataa	2160
agtatggtag	aggtaaaaac	atctatgtat	cctttttat	ctactcaagc	caggatgagg	2220
actgggtaag	aatgagacta	gtaaagaatt	tagaagaagg	ggtgcctcca	tttcagctct	2280
gccttcacta	cagagacttt	attcccggtg	tggccattgc	tgccaacatc	atccatgaag	2340
gtttccataa	aagccgaaag	gtgattgttg	tgggttccca	gcacttcatc	cagagccgct	2400
ggtgtatctt	tgaatatgag	attgctcaga	cctggcagtt	tctgagcagt	cgtgctggta	2460
tcatcttcat	tgtcctgcag	aagggtggaga	agaccctgct	caggcagcag	gtggagctgt	2520
accgccttct	cagcaggaac	acttacctgg	agtgggagga	cagtgtcctg	gggcggcaca	2580
tcttctggag	acgactcaga	aaagccctgc	tggatggtaa	atcatggaaat	ccagaaggaa	2640
cagtgggtac	aggatgcaat	tggcaggaag	caacatctat	ctgaagagga	aaaataaaaa	2700
cctcctgagg	catttcttgc	ccagctgggt	ccaacacttg	ttcagttaat	aagtattaaa	2760
tgctgccaca	tgtcaggcct	tatgctaagg	gtgagtaatt	ccatggtgca	ctagatatgc	2820
agggctgcta	atctcaagga	gcttccagtg	cagagggaaat	aaatgctaga	ctaaaataca	2880
gagtcttcca	ggtggcatt	tcaaccaact	cagtcaagga	acccatgaca	aagaaagtca	2940
tttcaactct	tacctcatca	agttgaataa	agacagagaa	aacagaaaga	gacattttc	3000

## 58182US002.ST25.txt

ttttcctgag	tctttgaat	ggaaattgta	ttatgttata	gccatcataa	aaccatttg	3060
gtagtttga	ctgaactggg	tgttcacttt	ttcccttttgc	attgaataca	atttaaattc	3120
tacccatgtga	ctgcagtcgt	caaggggctc	ctgatgcaag	atgccccttc	cattttaaatgt	3180
ctgtctccctt	acagaggtaa	aagtctaattg	gctaattcct	aaggaaacct	gattaacaca	3240
tgctcacaac	catcctggtc	attctcgaaac	atgttctatt	ttttaactaa	tcacccctga	3300
tatattttta	tttttatata	tccagtttgc	attttttac	gtcttgccta	taagctaata	3360
tcataaataa	ggttgtttaa	gacgtgcttc	aaatatccat	attaaccact	atttttcaag	3420
gaagtatgga	aaagtacact	ctgtcaatttgc	gtcactcgt	gtcattccaa	agtttattgccc	3480
tactaagttaa	tgactgtcat	gaaaggcagca	ttgaaataat	ttgtttaaag	ggggcactct	3540
tttaaacggg	aagaaaattt	ccgcttcctg	gtcttatcat	ggacaatttg	ggctataggc	3600
atgaaggaag	tgggattacc	ttaggaagtc	acctttctt	gattccagaa	acatatggc	3660
tgataaacc	gggggtgac	catgaaatga	gttgcagcag	atgtttat	ttttcagaac	3720
aagtgtatgtt	tgtatggac	atgaatctat	ttagggagac	acagatggct	gggatccctc	3780
ccctgtaccc	ttctca	tgtacca	caggagaact	a		3811

<210> 8  
<211> 799  
<212> PRT  
<213> Homo sapiens  
<400> 8

Met Glu Leu Asn Phe Tyr Lys Ile Pro Asp Asn Leu Pro Phe Ser Thr  
1 5 10 15

Lys Asn Leu Asp Leu Ser Phe Asn Pro Leu Arg His Leu Gly Ser Tyr  
20 25 30

Ser Phe Phe Ser Phe Pro Glu Leu Gln Val Leu Asp Leu Ser Arg Cys  
35 40 45

Glu Ile Gln Thr Ile Glu Asp Gly Ala Tyr Gln Ser Leu Ser His Leu  
50 55 60

Ser Thr Leu Ile Leu Thr Gly Asn Pro Ile Gln Ser Leu Ala Leu Gly  
65 70 75 80

Ala Phe Ser Gly Leu Ser Ser Leu Gln Lys Leu Val Ala Val Glu Thr  
85 90 95

Asn Leu Ala Ser Leu Glu Asn Phe Pro Ile Gly His Leu Lys Thr Leu  
100 105 110

## 58182US002.ST25.txt

Lys Glu Leu Asn Val Ala His Asn Leu Ile Gln Ser Phe Lys Leu Pro  
115 120 125

Glu Tyr Phe Ser Asn Leu Thr Asn Leu Glu His Leu Asp Leu Ser Ser  
130 135 140

Asn Lys Ile Gln Ser Ile Tyr Cys Thr Asp Leu Arg Val Leu His Gln  
145 150 155 160

Met Pro Leu Leu Asn Leu Ser Leu Asp Leu Ser Leu Asn Pro Met Asn  
165 170 175

Phe Ile Gln Pro Gly Ala Phe Lys Glu Ile Arg Leu His Lys Leu Thr  
180 185 190

Leu Arg Asn Asn Phe Asp Ser Leu Asn Val Met Lys Thr Cys Ile Gln  
195 200 205

Gly Leu Ala Gly Leu Glu Val His Arg Leu Val Leu Gly Glu Phe Arg  
210 215 220

Asn Glu Gly Asn Leu Glu Lys Phe Asp Lys Ser Ala Leu Glu Gly Leu  
225 230 235 240

Cys Asn Leu Thr Ile Glu Glu Phe Arg Leu Ala Tyr Leu Asp Tyr Tyr  
245 250 255

Leu Asp Asp Ile Ile Asp Leu Phe Asn Cys Leu Thr Asn Val Ser Ser  
260 265 270

Phe Ser Leu Val Ser Val Thr Ile Glu Arg Val Lys Asp Phe Ser Tyr  
275 280 285

Asn Phe Gly Trp Gln His Leu Glu Leu Val Asn Cys Lys Phe Gly Gln  
290 295 300

Phe Pro Thr Leu Lys Leu Lys Ser Leu Lys Arg Leu Thr Phe Thr Ser  
305 310 315 320

Asn Lys Gly Gly Asn Ala Phe Ser Glu Val Asp Leu Pro Ser Leu Glu  
325 330 335

Phe Leu Asp Leu Ser Arg Asn Gly Leu Ser Phe Lys Gly Cys Cys Ser  
340 345 350

Gln Ser Asp Phe Gly Thr Thr Ser Leu Lys Tyr Leu Asp Leu Ser Phe

58182us002.ST25.txt

355	360	365
Asn Gly Val Ile Thr Met Ser Ser Asn Phe Leu Gly Leu Glu Gln Leu 370                   375                   380		
Glu His Leu Asp Phe Gln His Ser Asn Leu Lys Gln Met Ser Glu Phe 385                   390                   395                   400		
Ser Val Phe Leu Ser Leu Arg Asn Leu Ile Tyr Leu Asp Ile Ser His 405                   410                   415		
Thr His Thr Arg Val Ala Phe Asn Gly Ile Phe Asn Gly Leu Ser Ser 420                   425                   430		
Leu Glu Val Leu Lys Met Ala Gly Asn Ser Phe Gln Glu Asn Phe Leu 435                   440                   445		
Pro Asp Ile Phe Thr Glu Leu Arg Asn Leu Thr Phe Leu Asp Leu Ser 450                   455                   460		
Gln Cys Gln Leu Glu Gln Leu Ser Pro Thr Ala Phe Asn Ser Leu Ser 465                   470                   475                   480		
Ser Leu Gln Val Leu Asn Met Ser His Asn Asn Phe Phe Ser Leu Asp 485                   490                   495		
Thr Phe Pro Tyr Lys Cys Leu Asn Ser Leu Gln Val Leu Asp Tyr Ser 500                   505                   510		
Leu Asn His Ile Met Thr Ser Lys Lys Gln Glu Leu Gln His Phe Pro 515                   520                   525		
Ser Ser Leu Ala Phe Leu Asn Leu Thr Gln Asn Asp Phe Ala Cys Thr 530                   535                   540		
Cys Glu His Gln Ser Phe Leu Gln Trp Ile Lys Asp Gln Arg Gln Leu 545                   550                   555                   560		
Leu Val Glu Val Glu Arg Met Glu Cys Ala Thr Pro Ser Asp Lys Gln 565                   570                   575		
Gly Met Pro Val Leu Ser Leu Asn Ile Thr Cys Gln Met Asn Lys Thr 580                   585                   590		
Ile Ile Gly Val Ser Val Leu Ser Val Leu Val Val Ser Val Val Ala 595                   600                   605		

## 58182US002.ST25.txt

Val Leu Val Tyr Lys Phe Tyr Phe His Leu Met Leu Leu Ala Gly Cys  
610 615 620

Ile Lys Tyr Gly Arg Gly Glu Asn Ile Tyr Asp Ala Phe Val Ile Tyr  
625 630 635 640

Ser Ser Gln Asp Glu Asp Trp Val Arg Asn Glu Leu Val Lys Asn Leu  
645 650 655

Glu Glu Gly Val Pro Pro Phe Gln Leu Cys Leu His Tyr Arg Asp Phe  
660 665 670

Ile Pro Gly Val Ala Ile Ala Ala Asn Ile Ile His Glu Gly Phe His  
675 680 685

Lys Ser Arg Lys Val Ile Val Val Val Ser Gln His Phe Ile Gln Ser  
690 695 700

Arg Trp Cys Ile Phe Glu Tyr Glu Ile Ala Gln Thr Trp Gln Phe Leu  
705 710 715 720

Ser Ser Arg Ala Gly Ile Ile Phe Ile Val Leu Gln Lys Val Glu Lys  
725 730 735

Thr Leu Leu Arg Gln Gln Val Glu Leu Tyr Arg Leu Leu Ser Arg Asn  
740 745 750

Thr Tyr Leu Glu Trp Glu Asp Ser Val Leu Gly Arg His Ile Phe Trp  
755 760 765

Arg Arg Leu Arg Lys Ala Leu Leu Asp Gly Lys Ser Trp Asn Pro Glu  
770 775 780

Gly Thr Val Gly Thr Gly Cys Asn Trp Gln Glu Ala Thr Ser Ile  
785 790 795

<210> 9

<211> 1261

<212> DNA

<213> Homo sapiens

<400> 9

tgttgtggatg tttttgaggg actttctcat cttcaagttc tgtatggaa tcataactat 60

cttaattccc ttccaccagg agtatttagc catctgactg cattaagggg actaaggcctc 120

aactccaaca ggctgacagt tctttctcac aatgatttac ctgctaattt agagatcctg 180

gacatatcca ggaaccagct cctagctcct aatcctgatg tatttgatc acttagtgtc 240

ttggatataa ctcataacaa gttcatttgatg gaatgtgaac tttagcacttt tatcaattgg 300

## 58182US002.ST25.txt

cttaatcaca ccaatgtcac tatacgctggg cctccctgcag acatatatgg tgtgtaccct	360
gactcggttct ctggggtttc cctcttctct ctttccacgg aagggttgtga tgaagaggaa	420
gtcttaaagt ccctaaagtt ctcccctttc attgtatgca ctgtcactct gactctgttc	480
ctcatgacca tcctcacagt cacaaagttc cggggcttct gtttatctg ttataagaca	540
gcccgagac tgggttcaa ggaccatccc cagggcacag aacctgatat gtacaaatat	600
gatgcctatt tgtgcttcag cagcaaagac ttcacatggg tgcaaatgc tttgctaaa	660
cacctggaca ctcaatacag tgacaaaaac agattcaacc tgtgcttga agaaagagac	720
tttgcctccag gagaaaaaccg cattgccaat atccaggatg ccattggaa cagtagaaag	780
atcggttgc ttgtgagcag acacttcctt agagatggct ggtgccttga agccttcagt	840
tatgcccagg gcaggtgctt atctgacctt aacagtgctc tcattatggt ggtgggttggg	900
tccttgcccc agtaccagtt gatgaaacat caatccatca gaggcttgc acagaaacag	960
cagtatttga ggtggccctga ggatctccag gatgtggct ggtttcttca taaactctct	1020
caacagatac taaagaaaga aaaagaaaag aagaaagaca ataacattcc gttgcaaact	1080
gtagcaacca tctccataatc aaaggagcaa tttccaactt atctcaagcc acaaataact	1140
cttcactttt tatttgccacc aagttatcat tttgggtcc tctctggagg tttttttttt	1200
ctttttgcta ctatgaaaac aacataaaatc tctcaatttt cgtatcaaaa aaaaaaaaaa	1260
a	1261

&lt;210&gt; 10

&lt;211&gt; 204

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 10

Met Thr Ile Leu Thr Val Thr Lys Phe Arg Gly Phe Cys Phe Ile Cys			
1	5	10	15

Tyr Lys Thr Ala Gln Arg Leu Val Phe Lys Asp His Pro Gln Gly Thr		
20	25	30

Glu Pro Asp Met Tyr Lys Tyr Asp Ala Tyr Leu Cys Phe Ser Ser Lys		
35	40	45

Asp Phe Thr Trp Val Gln Asn Ala Leu Leu Lys His Leu Asp Thr Gln		
50	55	60

Tyr Ser Asp Gln Asn Arg Phe Asn Leu Cys Phe Glu Glu Arg Asp Phe			
65	70	75	80

## 58182US002.ST25.txt

Val Pro Gly Glu Asn Arg Ile Ala Asn Ile Gln Asp Ala Ile Trp Asn  
 85 90 95

Ser Arg Lys Ile Val Cys Leu Val Ser Arg His Phe Leu Arg Asp Gly  
 100 105 110

Trp Cys Leu Glu Ala Phe Ser Tyr Ala Gln Gly Arg Cys Leu Ser Asp  
 115 120 125

Leu Asn Ser Ala Leu Ile Met Val Val Val Gly Ser Leu Ser Gln Tyr  
 130 135 140

Gln Leu Met Lys His Gln Ser Ile Arg Gly Phe Val Gln Lys Gln Gln  
 145 150 155 160

Tyr Leu Arg Trp Pro Glu Asp Leu Gln Asp Val Gly Trp Phe Leu His  
 165 170 175

Lys Leu Ser Gln Gln Ile Leu Lys Lys Glu Lys Glu Lys Lys Lys Asp  
 180 185 190

Asn Asn Ile Pro Leu Gln Thr Val Ala Thr Ile Ser  
 195 200

<210> 11

<211> 2753

<212> DNA

<213> Homo sapiens

<400> 11

agaatttgga	ctcatatcaa	gatgctctga	agaagaacaa	cccttttagga	tagccactgc	60
aacatcatga	ccaaagacaa	agaacctatt	gttaaaagct	tccattttgt	ttgccttatg	120
atcataatag	ttggAACCCAG	aatccagttc	tccgacggaa	atgaatttgc	agtagacaag	180
tcaaaaagag	gtcttattca	tgttccaaaa	gacctaccgc	tgaaaaccaa	agtcttagat	240
atgtctcaga	actacatcg	tgagcttcag	gtctctgaca	tgagcttct	atcagagttg	300
acagtttga	gactttccc	taacagaatc	cagctacttg	attnaagtgt	tttcaagttc	360
aaccaggatt	tagaatattt	ggatttatct	cataatcagt	tgcaaaagat	atccctgccat	420
cctattgtga	gtttcaggca	tttagatctc	tcattcaatg	atttcaaggc	cctgcccac	480
tgtaaaggat	ttggcaactt	atcacaactg	aatttcttgg	gattgagtgc	tatgaagctg	540
caaaaattag	atttgctgcc	aattgctcac	ttgcacatcaa	gttatatcct	tctggattta	600
agaaatttatt	atataaaaaga	aatgagaca	gaaagtctac	aaattctgaa	tgcaaaaacc	660
cttcaccc	ttttcaccc	aactagttt	ttcgctatcc	aagtgaacat	atcagttat	720
acttttagggt	gcttacaact	gactaatatt	aaattgaatg	atgacaactg	tcaagtttc	780

## 58182US002.ST25.txt

attaaaatTTT tatcagaact caccagaggt tcaacccTAC tgaATTTAC cctcaaccAC	840
atagaaacGA cttggAAATG CCTGGTCAGA GTCTTCAAT TTCTTGGCC CAAACCTGTG	900
gaatATCTCA atATTACAAT TTAAACAATA ATTGAAAGCA TTCGTGAAGA AGATTTACT	960
tattCTAAA CGACATTGAA AGCATTGACA ATAGAACATA TCACGAACCA AGTTTTCTG	1020
TTTTcacAGA cAGCTTGTA CACCCTGTTT TCTGAGATGA ACATTATGAT GTTAACCATT	1080
TcAGATAcac CTTTATAcA CATGCTGTGT CCTCATGCAC CAAGCACATT CAAGTTTTG	1140
AACtTTACCC AGAACGTTT CACAGATAGT ATTTTGAAA AATGTTCCAC GTTAGTTAAA	1200
TTGGAGACAC TTATCTTACA AAAAATGGA TTAAAAGACC TTTCAAAGT AGGTCTCATG	1260
ACGAAGGATA TGCCCTCTT GGAAATACTG GATGTTAGCT GGAATTCTT GGAATCTGGT	1320
AGACATAAAG AAAACTGCAC TTGGGTTGAG AGTATAGTGG TGTTAAATT GTCTCAAAT	1380
ATGCTTACTG ACTCTGTTT CAGATGTTA CCTCCCAGGA TCAAGGTACT TGATCTTCAC	1440
AGCAATAAAA TAAAGAGCGT TCCTAAACAA GTCGTTAAAC TGGAGCTT GCAAGAACTC	1500
AATGTTGCTT TCAATTCTTT ACTGACCTT CCTGGATGTG GCAGCTTGT CAGCCTTCT	1560
GtATTGATCA TTGATCACAA TTCAGTTCC CACCCATCGG CTGATTCTT CCAGAGCTGC	1620
CAGAAGATGA GGTCAATAAA AGCAGGGGAC AATCCATTCC AATGTACCTG TGAGCTAAGA	1680
GAATTGTCA AAAATATAGA CCAAGTATCA AGTGAAGTGT TAGAGGGCTG GCCTGATTCT	1740
TATAAGTGTG ACTACCCAGA AAGTTATAGA GGAAGCCCAC TAAAGGACTT TCACATGTCT	1800
GAATTATCCT GCAACATAAC TCTGCTGATC GTCACCATCG GTGCCACCAT GCTGGTGTG	1860
GCTGTGACTG TGACCTCCCT CTGCTAC TtgatCTGC CCTGGTATCT CAGGATGGTG	1920
TGCCAGTGGA CCCAGACTCG GCGCAGGGCC AGGAACATAC CCTAGAAGA ACTCCAAGA	1980
AACCTCCAGT TTGATGCTT TATTCATAT AGTGAACATG ATTCTGCCTG GGTGAAAAGT	2040
GAATTGGTAC CTTACCTAGA AAAAGAAGAT ATACAGATT GTCTTCATGA GAGGAACCTT	2100
GTCCTGGCA AGAGCATTGT GGAAAATATC ATCAACTGCA TTGAGAAGAG TTACAAGTCC	2160
ATCTTGTtt TGTCTCCAA CTTTGTCCAG AGTGAAGTGT GCCATTACGA ACTCTATTt	2220
GCCCATCACA ATCTCTTCA TGAAGGATCT AATAACTAA TCCTCATCTT ACTGGAACCC	2280
ATTCCACAGA ACAGCATTCC CAACAAGTAC CACAAGCTGA AGGCTCTCAT GACGCAGCGG	2340
ACTTATTTGC AGTGGCCAA GGAGAAAAGC AAACGTGGC TCTTTGGC TAACATTAGA	2400
GCCGCTTTA ATATGAAATT AACACTAGTC ACTGAAAACA ATGATGTGAA ATCTTAAAAAA	2460
AATTAGGAA ATTCAACTTA AGAAACCATT ATTACTTGG ATGATGGTGA ATAGTACAGT	2520
CGTAAGTAAC TGTCTGGAGG TGCCCTCATT ATCCTCATGC CTTCAAGGAAA GACTTAACAA	2580
AAACAAATGTT TCATCTGGGG AACTGAGCTA GGCAGGTGAGG TTAGCCTGCC AGTTAGAGAC	2640

58182US002.ST25.txt

agcccagtct	cttctggttt	aatcattatg	tttcaaattg	aaacagtctc	tttgagtaa	2700
atgctcagg	tttcagctcc	tctccactct	gctttcccaa	atggattctg	ttg	2753

<210> 12  
<211> 796  
<212> PRT  
<213> Homo sapiens

<400> 12

Met Thr Lys Asp Lys Glu Pro Ile Val Lys Ser Phe His Phe Val Cys  
1 5 10 15

Leu Met Ile Ile Ile Val Gly Thr Arg Ile Gln Phe Ser Asp Gly Asn  
20 25 30

Glu Phe Ala Val Asp Lys Ser Lys Arg Gly Leu Ile His Val Pro Lys  
35 40 45

Asp Leu Pro Leu Lys Thr Lys Val Leu Asp Met Ser Gln Asn Tyr Ile  
50 55 60

Ala Glu Leu Gln Val Ser Asp Met Ser Phe Leu Ser Glu Leu Thr Val  
65 70 75 80

Leu Arg Leu Ser His Asn Arg Ile Gln Leu Leu Asp Leu Ser Val Phe  
85 90 95

Lys Phe Asn Gln Asp Leu Glu Tyr Leu Asp Leu Ser His Asn Gln Leu  
100 105 110

Gln Lys Ile Ser Cys His Pro Ile Val Ser Phe Arg His Leu Asp Leu  
115 120 125

Ser Phe Asn Asp Phe Lys Ala Leu Pro Ile Cys Lys Glu Phe Gly Asn  
130 135 140

Leu Ser Gln Leu Asn Phe Leu Gly Leu Ser Ala Met Lys Leu Gln Lys  
145 150 155 160

Leu Asp Leu Leu Pro Ile Ala His Leu His Leu Ser Tyr Ile Leu Leu  
165 170 175

Asp Leu Arg Asn Tyr Tyr Ile Lys Glu Asn Glu Thr Glu Ser Leu Gln  
180 185 190

Ile Leu Asn Ala Lys Thr Leu His Leu Val Phe His Pro Thr Ser Leu  
195 200 205

## 58182US002.ST25.txt

Phe Ala Ile Gln Val Asn Ile Ser Val Asn Thr Leu Gly Cys Leu Gln  
210 215 220

Leu Thr Asn Ile Lys Leu Asn Asp Asp Asn Cys Gln Val Phe Ile Lys  
225 230 235 240

Phe Leu Ser Glu Leu Thr Arg Gly Ser Thr Leu Leu Asn Phe Thr Leu  
245 250 255

Asn His Ile Glu Thr Thr Trp Lys Cys Leu Val Arg Val Phe Gln Phe  
260 265 270

Leu Trp Pro Lys Pro Val Glu Tyr Leu Asn Ile Tyr Asn Leu Thr Ile  
275 280 285

Ile Glu Ser Ile Arg Glu Glu Asp Phe Thr Tyr Ser Lys Thr Thr Leu  
290 295 300

Lys Ala Leu Thr Ile Glu His Ile Thr Asn Gln Val Phe Leu Phe Ser  
305 310 315 320

Gln Thr Ala Leu Tyr Thr Val Phe Ser Glu Met Asn Ile Met Met Leu  
325 330 335

Thr Ile Ser Asp Thr Pro Phe Ile His Met Leu Cys Pro His Ala Pro  
340 345 350

Ser Thr Phe Lys Phe Leu Asn Phe Thr Gln Asn Val Phe Thr Asp Ser  
355 360 365

Ile Phe Glu Lys Cys Ser Thr Leu Val Lys Leu Glu Thr Leu Ile Leu  
370 375 380

Gln Lys Asn Gly Leu Lys Asp Leu Phe Lys Val Gly Leu Met Thr Lys  
385 390 395 400

Asp Met Pro Ser Leu Glu Ile Leu Asp Val Ser Trp Asn Ser Leu Glu  
405 410 415

Ser Gly Arg His Lys Glu Asn Cys Thr Trp Val Glu Ser Ile Val Val  
420 425 430

Leu Asn Leu Ser Ser Asn Met Leu Thr Asp Ser Val Phe Arg Cys Leu  
435 440 445

Pro Pro Arg Ile Lys Val Leu Asp Leu His Ser Asn Lys Ile Lys Ser  
450 455 460

## 58182US002.ST25.txt

Val Pro Lys Gln Val Val Lys Leu Glu Ala Leu Gln Glu Leu Asn Val  
465 470 475 480

Ala Phe Asn Ser Leu Thr Asp Leu Pro Gly Cys Gly Ser Phe Ser Ser  
485 490 495

Leu Ser Val Leu Ile Ile Asp His Asn Ser Val Ser His Pro Ser Ala  
500 505 510

Asp Phe Phe Gln Ser Cys Gln Lys Met Arg Ser Ile Lys Ala Gly Asp  
515 520 525

Asn Pro Phe Gln Cys Thr Cys Glu Leu Arg Glu Phe Val Lys Asn Ile  
530 535 540

Asp Gln Val Ser Ser Glu Val Leu Glu Gly Trp Pro Asp Ser Tyr Lys  
545 550 555 560

Cys Asp Tyr Pro Glu Ser Tyr Arg Gly Ser Pro Leu Lys Asp Phe His  
565 570 575

Met Ser Glu Leu Ser Cys Asn Ile Thr Leu Leu Ile Val Thr Ile Gly  
580 585 590

Ala Thr Met Leu Val Leu Ala Val Thr Val Thr Ser Leu Cys Ile Tyr  
595 600 605

Leu Asp Leu Pro Trp Tyr Leu Arg Met Val Cys Gln Trp Thr Gln Thr  
610 615 620

Arg Arg Arg Ala Arg Asn Ile Pro Leu Glu Glu Leu Gln Arg Asn Leu  
625 630 635 640

Gln Phe His Ala Phe Ile Ser Tyr Ser Glu His Asp Ser Ala Trp Val  
645 650 655

Lys Ser Glu Leu Val Pro Tyr Leu Glu Lys Glu Asp Ile Gln Ile Cys  
660 665 670

Leu His Glu Arg Asn Phe Val Pro Gly Lys Ser Ile Val Glu Asn Ile  
675 680 685

Ile Asn Cys Ile Glu Lys Ser Tyr Lys Ser Ile Phe Val Leu Ser Pro  
690 695 700

Asn Phe Val Gln Ser Glu Trp Cys His Tyr Glu Leu Tyr Phe Ala His

58182US002.ST25.txt

705	710	715	720
His Asn Leu Phe His Glu Gly Ser Asn Asn Leu Ile Leu Ile Leu Leu 725                                   730                           735			
Glu Pro Ile Pro Gln Asn Ser Ile Pro Asn Lys Tyr His Lys Leu Lys 740                                   745                           750			
Ala Leu Met Thr Gln Arg Thr Tyr Leu Gln Trp Pro Lys Glu Lys Ser 755                                   760                           765			
Lys Arg Gly Leu Phe Trp Ala Asn Ile Arg Ala Ala Phe Asn Met Lys 770                                   775                           780			
Leu Thr Leu Val Thr Glu Asn Asn Asp Val Lys Ser 785                                   790                           795			

<210> 13  
<211> 5007  
<212> DNA  
<213> Homo sapiens

<400> 13

actccagata	taggatca	ccatgccatc	aagaaagt	tg atgctattgg	gcccac	tctca	60				
agctgatctt	ggcac	cctctc	atgctctg	ctcttcaacc	agac	ctctac	attccat	ttt	120		
ggaagaagac	taaaaat	gggt	tttccaat	tg	ggacact	ga	agagaca	aaat	180		
ttaacataa	tcctaattt	c	aaactc	ctt	gggct	tagat	g	tttc	ctaa	240	
tgtgatgtca	ctctggatgt	tccaaaga	ac	catgtgat	cg	tggactgc	ac	agacaag	cat	300	
ttgacagaaa	ttcctggagg	tatt	cccac	g	aacacc	acg	acctc	acc	caccatta	360	
cacataccag	acat	ctcccc	agcgt	cc	cac	actgg	accat	ctg	gt	420	
ttcagatgca	actgtgtacc	tatt	ccact	g	ggtca	aaaaa	aca	acat	gtg	480	
ctgcagatta	aacccaga	ag	ctt	tagt	gga	ctc	actt	tatt	aaaat	ccct	540
ggaaacc	actag	at	acc	gcagg	gc	ctcc	gc	ct	tct	cag	600
gaggccaaca	acat	ctttt	c	atc	gaaaa	g	aga	atct	aa	caga	660
atactctacc	tgg	ccaaaa	ct	gtt	tattat	c	gaa	atc	tt	ttc	720
gagaaagatg	c	ttc	c	t	ttg	aca	ag	taa	gt	tc	780
gtcacagccg	tcc	c	t	ttt	g	ccat	c	t	ttt	ct	840
atgattgcaa	aaat	ccaaga	ag	atg	at	ttt	a	taa	cc	tgc	900
ctaagtggaa	att	gc	c	t	ttg	tata	at	g	cc	tg	960
aattctcccc	tacagat	ccc	t	gt	aaat	gct	ttt	gt	tg	cg	1020

58182US002.ST25.txt

cgtctacaca	gtaactctct	tcagcatgtg	cccccaagat	ggttaagaa	catcaacaaa	1080
ctccaggaac	tggatctgtc	ccaaaacttc	ttggccaaag	aaattgggga	tgctaaattt	1140
ctgcatttc	tcccagcct	catccaattt	gatctgtctt	tcaattttga	acttcaggc	1200
tatcgcat	ctatgaatct	atcacaaggca	ttttcttcac	tgaaaagcct	gaaaattctg	1260
cggatcagag	gatatgtctt	taaagagttt	aaaagctta	acctctcgcc	attacataat	1320
cttcaaaatc	ttgaagttct	tгatcttggc	actaacttta	taaaaattgc	taacctcagc	1380
atgtttaaac	aattttaaag	actgaaagtc	atagatctt	cagtgaataa	aatatcacct	1440
tcaggagatt	caagtgaagt	tggcttctgc	tcaaatgcca	gaacttctgt	agaaaagttat	1500
gaaccccagg	tcctggaaca	attacattat	ttcagatatg	ataagtatgc	aaggagttgc	1560
agattcaaaa	acaaagaggc	ttctttcatg	tctgttaatg	aaagctgcta	caagtatggg	1620
cagaccttgg	atctaagtaa	aaatagtata	tttttgtca	agtccctctg	ttttcagcat	1680
ctttcttcc	tcaaatgcct	gaatctgtca	ggaaatctca	ttagccaaac	tcttaatggc	1740
agtgaattcc	aacctttagc	agagctgaga	tatttgact	tctccaacaa	ccggcttgat	1800
ttactccatt	caacagcatt	tgaagagctt	cacaaactgg	aagttctgga	tataaggcagt	1860
aatagccatt	atttcaatc	agaaggaatt	actcatatgc	taaactttac	caagaaccta	1920
aaggttctgc	agaaactgat	gatgaacgac	aatgacatct	cttcctccac	cagcaggacc	1980
atggagagt	agtctcttag	aactctggaa	ttcagaggaa	atcacttaga	tgttttatgg	2040
agagaaggt	ataacagata	cttacaatta	ttcaagaatc	tgctaaaatt	agaggaattha	2100
gacatctcta	aaaattccct	aagtttctt	ccttctggag	tttttgcattt	tatgcctcca	2160
aatctaaaga	atctctttt	ggccaaaaat	gggctcaaatt	ctttcagttt	gaagaaactc	2220
cagtgtctaa	agaacctgg	aactttggac	ctcagccaca	accaactgac	cactgtccct	2280
gagagattat	ccaaactgttc	cagaagcctc	aagaatctga	ttcttaagaa	taatcaaatc	2340
aggagtctga	cgaagtattt	tctacaagat	gccttccagt	tgcgatatct	ggatctcagc	2400
tcaaataaaa	tccagatgat	ccaaaagacc	agcttcccag	aaaatgtcct	caacaatctg	2460
aagatgttgc	ttttgcattca	taatcggttt	ctgtgcacct	gtgatgtgt	gtggtttgc	2520
tggtgggtta	accatacgga	ggtgactatt	ccttacctgg	ccacagatgt	gacttgtgt	2580
gggccaggag	cacacaaggg	ccaaagtgt	atctccctgg	atctgtacac	ctgtgagtt	2640
gatctgacta	acctgattct	gttctcactt	tccatatctg	tatctctctt	tctcatggtg	2700
atgtatgacag	caagtcaccc	ctatttctgg	gatgtgtggt	atatttacca	tttctgttaag	2760
gccaagataa	aggggtatca	gcgtctaata	tcaccagact	gttgctatga	tgcttttatt	2820
gtgtatgaca	ctaaagaccc	agctgtgacc	gagtgggttt	tggctgagct	ggtggccaaa	2880
ctggaagacc	caagagagaa	acattttat	ttatgtctcg	aggaaaggga	ctggttacca	2940

## 58182US002.ST25.txt

gggcagccag ttctggaaaa ccttccccag agcatacagc ttagcaaaaa gacagtgtt	3000
gtgatgacag acaagtatgc aaagactgaa aatttaaga tagcattta cttgtccat	3060
cagaggctca tggatgaaaa agttgatgtg attatcttga tatttcttga gaagccctt	3120
cagaagtcca agttcccca gctccggaaa aggctctgtg ggagttctgt ccttgagtgg	3180
ccaacaaacc cgcaagctca cccatacttc tggcagtgtc taaagaacgc cctggccaca	3240
gacaatcatg tggcctatag tcaggtgttc aaggaaacgg tctagccctt ctttgcaaaa	3300
cacaactgcc tagtttacca aggagaggcc tggctgttta aattgttttca atatatatca	3360
caccaaaagc gtgtttgaa attcttcaag aaatgagatt gcccatattt caggggagcc	3420
accaacgtct gtcacaggag ttggaaaagat ggggtttata taatgcatca agtcttctt	3480
cttatctctc tgtgtctcta tttgcacttg agtctctcac ctcagctcct gtaaaagagt	3540
ggcaagtaaa aaacatgggg ctctgattct cctgttaattt tgataattaa atatacacac	3600
aatcatgaca ttgagaagaa ctgcatttct acccttaaaa agtactggta tatacagaaa	3660
tagggtaaaa aaaaactcaa gctctctcta tatgagacca aaatgtacta gagtttagtt	3720
agtgaataaa aaaaccagtc agctggccgg gcatggtggc tcatgcttgt aatcccagca	3780
cttgggagg ccgaggcagg tggatcacga ggtcaggagt ttgagaccag tctggccaac	3840
atggtaaaac cccgtctgta ctaaaaatac aaaaatttgc tggcgtggt ggtgggtgcc	3900
tgtatccca gctacttggg aggctgaggc aggagaatcg cttaacccg ggaggtggag	3960
gtggcagtga gccgagatca cgcactgca atgcagcccg ggcaacagag ctagactgtc	4020
tcaaaaagaac aaaaaaaaaaa aaacacaaaaa aaactcagtc agttcttaa ccaattgttt	4080
ccgtgtcatc cagggccccca ttctgtcag attgagtgtg ggcaccacac aggtggttgc	4140
tgcctcagtg cttccgtctc ttttccttgc ggcctgcttc tgggttccat agggaaacag	4200
taagaaaagaa agacacatcc ttaccataaa tgcataatggt ccacctacaa atagaaaaat	4260
atttaaatga tctgccttta tacaaaagtga tattctctac ctttgataat ttacctgctt	4320
aaatgtttt atctgcactg caaagtactg tatccaaagt aaaatttccat catccaatat	4380
ctttcaaact gtttgttaa ctaatgcccattt atattgtaa gtatctgcac acttgatata	4440
gcaacgttag atggtttga tggtaaaccc taaaggagga ctccaaagagt gtgtatttt	4500
ttatagttt atcagagatg acaatttattt gaatgccaat tatatggatt cttttcattt	4560
tttgctggag gatggagaa gaaaccaaag tttatagacc ttcacattga gaaagcttca	4620
gtttgaact tcagctatca gattaaaaaa caacagaaag aaccaagaca ttcttaagat	4680
gcctgtactt tcagctgggt ataaattcat gagttcaaag attgaaacct gaccaatttg	4740
ctttatccatc tgaaagaagt gatctacaaa ggtgtttgtg ccatttgaa aacagcgtgc	4800

58182us002.ST25.txt

atgtgttcaa	gccttagatt	ggcgatgtcg	tatttcctc	acgtgtggca	atgccaagg	4860
ctttacttta	cctgtgagta	cacactatat	gaattatttc	caacgtacat	ttaatcaata	4920
agggtcacaa	attcccaaat	caatctctgg	aataaataga	gaggtaatta	aattgctgga	4980
gccaaactatt	tcacaacttc	tgtaagc				5007
<210>	14					
<211>	1049					
<212>	PRT					
<213>	Homo sapiens					
<400>	14					
Met Val Phe Pro Met Trp Thr Leu Lys Arg Gln Ile Leu Ile Leu Phe						
1	5	10		15		
Asn Ile Ile Leu Ile Ser Lys Leu Leu Gly Ala Arg Trp Phe Pro Lys						
20	25	30				
Thr Leu Pro Cys Asp Val Thr Leu Asp Val Pro Lys Asn His Val Ile						
35	40	45				
Val Asp Cys Thr Asp Lys His Leu Thr Glu Ile Pro Gly Gly Ile Pro						
50	55	60				
Thr Asn Thr Thr Asn Leu Thr Leu Thr Ile Asn His Ile Pro Asp Ile						
65	70	75	80			
Ser Pro Ala Ser Phe His Arg Leu Asp His Leu Val Glu Ile Asp Phe						
85	90	95				
Arg Cys Asn Cys Val Pro Ile Pro Leu Gly Ser Lys Asn Asn Met Cys						
100	105	110				
Ile Lys Arg Leu Gln Ile Lys Pro Arg Ser Phe Ser Gly Leu Thr Tyr						
115	120	125				
Leu Lys Ser Leu Tyr Leu Asp Gly Asn Gln Leu Leu Glu Ile Pro Gln						
130	135	140				
Gly Leu Pro Pro Ser Leu Gln Leu Leu Ser Leu Glu Ala Asn Asn Ile						
145	150	155	160			
Phe Ser Ile Arg Lys Glu Asn Leu Thr Glu Leu Ala Asn Ile Glu Ile						
165	170	175				
Leu Tyr Leu Gly Gln Asn Cys Tyr Tyr Arg Asn Pro Cys Tyr Val Ser						
180	185	190				

## 58182US002.ST25.txt

Tyr Ser Ile Glu Lys Asp Ala Phe Leu Asn Leu Thr Lys Leu Lys Val  
195 200 205

Leu Ser Leu Lys Asp Asn Asn Val Thr Ala Val Pro Thr Val Leu Pro  
210 215 220

Ser Thr Leu Thr Glu Leu Tyr Leu Tyr Asn Asn Met Ile Ala Lys Ile  
225 230 235 240

Gln Glu Asp Asp Phe Asn Asn Leu Asn Gln Leu Gln Ile Leu Asp Leu  
245 250 255

Ser Gly Asn Cys Pro Arg Cys Tyr Asn Ala Pro Phe Pro Cys Ala Pro  
260 265 270

Cys Lys Asn Asn Ser Pro Leu Gln Ile Pro Val Asn Ala Phe Asp Ala  
275 280 285

Leu Thr Glu Leu Lys Val Leu Arg Leu His Ser Asn Ser Leu Gln His  
290 295 300

Val Pro Pro Arg Trp Phe Lys Asn Ile Asn Lys Leu Gln Glu Leu Asp  
305 310 315 320

Leu Ser Gln Asn Phe Leu Ala Lys Glu Ile Gly Asp Ala Lys Phe Leu  
325 330 335

His Phe Leu Pro Ser Leu Ile Gln Leu Asp Leu Ser Phe Asn Phe Glu  
340 345 350

Leu Gln Val Tyr Arg Ala Ser Met Asn Leu Ser Gln Ala Phe Ser Ser  
355 360 365

Leu Lys Ser Leu Lys Ile Leu Arg Ile Arg Gly Tyr Val Phe Lys Glu  
370 375 380

Leu Lys Ser Phe Asn Leu Ser Pro Leu His Asn Leu Gln Asn Leu Glu  
385 390 395 400

Val Leu Asp Leu Gly Thr Asn Phe Ile Lys Ile Ala Asn Leu Ser Met  
405 410 415

Phe Lys Gln Phe Lys Arg Leu Lys Val Ile Asp Leu Ser Val Asn Lys  
420 425 430

Ile Ser Pro Ser Gly Asp Ser Ser Glu Val Gly Phe Cys Ser Asn Ala  
435 440 445

## 58182US002.ST25.txt

Arg Thr Ser Val Glu Ser Tyr Glu Pro Gln Val Leu Glu Gln Leu His  
450 455 460

Tyr Phe Arg Tyr Asp Lys Tyr Ala Arg Ser Cys Arg Phe Lys Asn Lys  
465 470 475 480

Glu Ala Ser Phe Met Ser Val Asn Glu Ser Cys Tyr Lys Tyr Gly Gln  
485 490 495

Thr Leu Asp Leu Ser Lys Asn Ser Ile Phe Phe Val Lys Ser Ser Asp  
500 505 510

Phe Gln His Leu Ser Phe Leu Lys Cys Leu Asn Leu Ser Gly Asn Leu  
515 520 525

Ile Ser Gln Thr Leu Asn Gly Ser Glu Phe Gln Pro Leu Ala Glu Leu  
530 535 540

Arg Tyr Leu Asp Phe Ser Asn Asn Arg Leu Asp Leu Leu His Ser Thr  
545 550 555 560

Ala Phe Glu Glu Leu His Lys Leu Glu Val Leu Asp Ile Ser Ser Asn  
565 570 575

Ser His Tyr Phe Gln Ser Glu Gly Ile Thr His Met Leu Asn Phe Thr  
580 585 590

Lys Asn Leu Lys Val Leu Gln Lys Leu Met Met Asn Asn Asp Ile  
595 600 605

Ser Ser Ser Thr Ser Arg Thr Met Glu Ser Glu Ser Leu Arg Thr Leu  
610 615 620

Glu Phe Arg Gly Asn His Leu Asp Val Leu Trp Arg Glu Gly Asp Asn  
625 630 635 640

Arg Tyr Leu Gln Leu Phe Lys Asn Leu Leu Lys Leu Glu Glu Leu Asp  
645 650 655

Ile Ser Lys Asn Ser Leu Ser Phe Leu Pro Ser Gly Val Phe Asp Gly  
660 665 670

Met Pro Pro Asn Leu Lys Asn Leu Ser Leu Ala Lys Asn Gly Leu Lys  
675 680 685

Ser Phe Ser Trp Lys Lys Leu Gln Cys Leu Lys Asn Leu Glu Thr Leu

58182US002.ST25.txt

690                    695                    700  
Asp Leu Ser His Asn Gln Leu Thr Thr Val Pro Glu Arg Leu Ser Asn  
705                    710                    715                    720  
  
Cys Ser Arg Ser Leu Lys Asn Leu Ile Leu Lys Asn Asn Gln Ile Arg  
725                    730                    735  
  
Ser Leu Thr Lys Tyr Phe Leu Gln Asp Ala Phe Gln Leu Arg Tyr Leu  
740                    745                    750  
  
Asp Leu Ser Ser Asn Lys Ile Gln Met Ile Gln Lys Thr Ser Phe Pro  
755                    760                    765  
  
Glu Asn Val Leu Asn Asn Leu Lys Met Leu Leu Leu His His Asn Arg  
770                    775                    780  
  
Phe Leu Cys Thr Cys Asp Ala Val Trp Phe Val Trp Trp Val Asn His  
785                    790                    795                    800  
  
Thr Glu Val Thr Ile Pro Tyr Leu Ala Thr Asp Val Thr Cys Val Gly  
805                    810                    815  
  
Pro Gly Ala His Lys Gly Gln Ser Val Ile Ser Leu Asp Leu Tyr Thr  
820                    825                    830  
  
Cys Glu Leu Asp Leu Thr Asn Leu Ile Leu Phe Ser Leu Ser Ile Ser  
835                    840                    845  
  
Val Ser Leu Phe Leu Met Val Met Met Thr Ala Ser His Leu Tyr Phe  
850                    855                    860  
  
Trp Asp Val Trp Tyr Ile Tyr His Phe Cys Lys Ala Lys Ile Lys Gly  
865                    870                    875                    880  
  
Tyr Gln Arg Leu Ile Ser Pro Asp Cys Cys Tyr Asp Ala Phe Ile Val  
885                    890                    895  
  
Tyr Asp Thr Lys Asp Pro Ala Val Thr Glu Trp Val Leu Ala Glu Leu  
900                    905                    910  
  
Val Ala Lys Leu Glu Asp Pro Arg Glu Lys His Phe Asn Leu Cys Leu  
915                    920                    925  
  
Glu Glu Arg Asp Trp Leu Pro Gly Gln Pro Val Leu Glu Asn Leu Ser  
930                    935                    940

## 58182US002.ST25.txt

Gln Ser Ile Gln Leu Ser Lys Lys Thr Val Phe Val Met Thr Asp Lys  
 945 950 955 960

Tyr Ala Lys Thr Glu Asn Phe Lys Ile Ala Phe Tyr Leu Ser His Gln  
 965 970 975

Arg Leu Met Asp Glu Lys Val Asp Val Ile Ile Leu Ile Phe Leu Glu  
 980 985 990

Lys Pro Phe Gln Lys Ser Lys Phe Leu Gln Leu Arg Lys Arg Leu Cys  
 995 1000 1005

Gly Ser Ser Val Leu Glu Trp Pro Thr Asn Pro Gln Ala His Pro  
 1010 1015 1020

Tyr Phe Trp Gln Cys Leu Lys Asn Ala Leu Ala Thr Asp Asn His  
 1025 1030 1035

Val Ala Tyr Ser Gln Val Phe Lys Glu Thr Val  
 1040 1045

<210> 15  
 <211> 3311  
 <212> DNA  
 <213> Homo sapiens

<400> 15						
ttctgcgtc	ctgcaagtta	cggaaatgaaa	aattagaaca	acagaaaacat	ggaaaacatg	60
tcccttcagt	cgtcaatgct	gacctgcatt	ttcctgctaa	tatctggttc	ctgtgaggtt	120
tgcgccgaag	aaaatttttc	tagaagctat	ccttgtatg	agaaaaagca	aatgactca	180
gttattgcag	agtgcagcaa	tcgtcgacta	caggaagttc	ccccaaacggt	gggcaaataat	240
gtgacagaac	tagacctgtc	tgataatttc	atcacacaca	taacgaatga	atcattcaa	300
gggctgcaaa	atctcactaa	aataaatcta	aaccacaacc	ccaatgtaca	gcaccagaac	360
ggaaatcccg	gtataacaatc	aaatggctt	aatatcacag	acggggcatt	cctcaaccta	420
aaaaacctaa	gggagttact	gcttgaagac	aaccaggttac	cccaaataacc	ctctggttt	480
ccagagtctt	tgacagaact	tagtctaatt	caaaaacaata	tatacaacat	aactaaagag	540
ggcatttcaa	gacttataaa	cttgaaaaat	ctctatttgg	ccttggactg	ctattttaac	600
aaagtttgcg	agaaaactaa	catagaagat	ggagttttt	aaacgctgac	aaatttgag	660
ttgctatcac	tatcttcaa	ttcttccca	cacgtgccac	ccaaactgccc	aagctcccta	720
cgcaaacttt	ttctgagcaa	cacccagatc	aaatacatta	gtgaagaaga	tttcaaggga	780
ttgataaatt	taacattact	agatttaagc	gggaactgtc	cgaggtgctt	caatgccccca	840
tttccatgcg	tgccttgc	tggggctgt	tcaattaata	tagatcgttt	tgctttcaa	900

## 58182US002.ST25.txt

aacctgaccc	aacttcgata	cctaaaccc	tctagcactt	ccctcaggaa	gattaatgct	960
gcctggttta	aaaatatgcc	tcatctgaag	gtgctggatc	ttgaattcaa	ctattttagtg	1020
ggagaaaatag	cctctggggc	attttaacg	atgctcccc	gcttagaaat	acttgacttg	1080
tcttttaact	atataaaggg	gagttatcca	cagcatatta	atattccag	aaacttctct	1140
aaacaaaaatgt	ctctacgggc	attgcattt	agaggttatg	tgttccagga	actcagagaa	1200
gatgatttcc	agcccctgat	gcagcttcca	aacttatcga	ctatcaactt	gggtattaat	1260
tttattaagc	aaatcgattt	caaacttttc	caaattttct	ccaatctgga	aattatttac	1320
ttgtcagaaa	acagaatatc	accgttggta	aaagataccc	ggcagagttt	tgcaaatagt	1380
tcctcttttc	aacgtcatat	ccggaaacga	cgctcaacag	attttgagtt	tgacccacat	1440
tcgaactttt	atcatttcac	ccgtccttta	ataaagccac	aatgtgctgc	ttatggaaaa	1500
gccttagatt	taagcctcaa	cagtattttc	ttcattgggc	caaaccattt	tgaaaatctt	1560
cctgacattt	cctgtttaaaa	tctgtctgca	aatagcaatg	ctcaagtgtt	aagtggaaact	1620
gaatttttag	ccattccctca	tgtcaaataat	ttggatttga	caaacaatag	actagacttt	1680
gataatgcta	gtgcttttac	tgaatttgtcc	gacttggaaag	ttcttagatct	cagctataat	1740
tcacactatt	tcagaatagc	aggcgtaaca	catcatctag	aattttattca	aaatttcaca	1800
aatctaaaag	ttttaaactt	gagccacaac	aacatttata	ctttaacaga	taagtataac	1860
ctggaaagca	agtccctgg	agaatttagtt	ttcagtggca	atcgccctgaa	cattttgtgg	1920
aatgatgatg	acaacaggta	tatctccattt	ttcaaaggtc	tcaagaatct	gacacgtctg	1980
gatttatccc	ttaataggct	gaagcacatc	ccaaatgaag	cattccttaa	tttgcacgc	2040
agtctcactg	aactacatat	aaatgataat	atgttaaagt	tttttaactg	gacattactc	2100
cagcagtccc	ctcgctcga	gttgcttgac	ttacgtggaa	acaaaactact	cttttaact	2160
gatagcctat	ctgactttac	atctccctt	cgacactgc	tgctgagtca	taacaggatt	2220
tcccacctac	cctctggctt	tctttctgaa	gtcagtagtc	tgaagcacct	cgatttaagt	2280
tccaaatctgc	taaaaacaat	caacaaatcc	gcacttggaa	ctaagaccac	caccaaaatta	2340
tctatgttgg	aactacacgg	aaaccccttt	gaatgcacct	gtgacattgg	agatttccga	2400
agatggatgg	atgaacatct	gaatgtcaaa	attcccagac	tggtagatgt	catttgcgtcc	2460
agtccctgggg	atcaaagagg	gaagagtatt	gtgagctgg	agctgacaac	ttgtgtttca	2520
gatgtcactg	cagtatattt	atttttcttc	acgttctta	tcaccaccat	ggttatgttg	2580
gctgccctgg	ctcaccat	gtttactgg	gatgttggt	ttatatataa	tgtgtgttta	2640
gctaaggtaa	aaggctacag	gtctcttcc	acatccaaa	cttctatga	tgcttacatt	2700
tcttatgaca	ccaaagatgc	ctctgttact	gactgggtga	taaatgagct	gcgctaccac	2760

58182US002.ST25.txt	
cttgaagaga	2820
gccgagacaa	
aacacgttctc	
ctttgtctag	
aggagagggta	
ttggggaccccg	
ggattggcca	2880
tcatcgacaa	
cctcatgcag	
agcatcaacc	
aaagcaagaa	
aacagtatTTT	
gttttaacca	2940
aaaaaatatgc	
aaaaagctgg	
aactttaaaa	
cagctttta	
cttggctttg	
cagaggctaa	3000
tggatgagaa	
catggatgtg	
attatattta	
tcctgctgga	
gccagtgtta	
cagcattctc	3060
agtatTTGAG	
gctacggcag	
cgatatCTGTA	
agagCTCCAT	
cctccAGTGG	
cctgacaacc	3120
cgaaggcaga	
aggctgttt	
tggcaaactc	
tgagaaatgt	
ggTCttGACT	
gaaaatgatt	3180
cacggtataa	
caatatgtat	
gtcgattCCA	
ttaAGCAATA	
ctaACTGACG	
ttaAGTCATG	3240
atTCGCGCC	
ataataaaga	
tgcaaaggaa	
tgacatttct	
gtatttagtta	
tctattgcta	3300
tgtAACAAAT	
tatcccAAAAA	
cttagtggtt	
taaaACAACA	
catttGCTGG	
cccacAGTTT	3311
T	

<210> 16  
<211> 1041  
<212> PRT  
<213> Homo sapiens  
  
<400> 16

Met Glu Asn Met Phe Leu Gln Ser Ser Met Leu Thr Cys Ile Phe Leu  
1 5 10 15

Leu Ile Ser Gly Ser Cys Glu Leu Cys Ala Glu Glu Asn Phe Ser Arg  
20 25 30

Ser Tyr Pro Cys Asp Glu Lys Lys Gln Asn Asp Ser Val Ile Ala Glu  
35 40 45

Cys Ser Asn Arg Arg Leu Gln Glu Val Pro Gln Thr Val Gly Lys Tyr  
50 55 60

val Thr Glu Leu Asp Leu Ser Asp Asn Phe Ile Thr His Ile Thr Asn  
65 . . . 70 . . . 75 . . . 80

Glu Ser Phe Gln Gln Gly Leu Gln Asn Leu Thr Lys Ile Asn Leu Asn His  
85 90 95

Asn Pro Asn Val Gln His Gln Asn Gly Asn Pro Gly Ile Gln Ser Asn  
100 105 110

Gly Leu Asn Ile Thr Asp Gly Ala Phe Leu Asn Leu Lys Asn Leu Arg  
115 120 125

## 58182US002.ST25.txt

Pro Glu Ser Leu Thr Glu Leu Ser Leu Ile Gln Asn Asn Ile Tyr Asn  
145 150 155 160

Ile Thr Lys Glu Gly Ile Ser Arg Leu Ile Asn Leu Lys Asn Leu Tyr  
165 170 175

Leu Ala Trp Asn Cys Tyr Phe Asn Lys Val Cys Glu Lys Thr Asn Ile  
180 185 190

Glu Asp Gly Val Phe Glu Thr Leu Thr Asn Leu Glu Leu Leu Ser Leu  
195 200 205

Ser Phe Asn Ser Leu Ser His Val Pro Pro Lys Leu Pro Ser Ser Leu  
210 215 220

Arg Lys Leu Phe Leu Ser Asn Thr Gln Ile Lys Tyr Ile Ser Glu Glu  
225 230 235 240

Asp Phe Lys Gly Leu Ile Asn Leu Thr Leu Leu Asp Leu Ser Gly Asn  
245 250 255

Cys Pro Arg Cys Phe Asn Ala Pro Phe Pro Cys Val Pro Cys Asp Gly  
260 265 270

Gly Ala Ser Ile Asn Ile Asp Arg Phe Ala Phe Gln Asn Leu Thr Gln  
275 280 285

Leu Arg Tyr Leu Asn Leu Ser Ser Thr Ser Leu Arg Lys Ile Asn Ala  
290 295 300

Ala Trp Phe Lys Asn Met Pro His Leu Lys Val Leu Asp Leu Glu Phe  
305 310 315 320

Asn Tyr Leu Val Gly Glu Ile Ala Ser Gly Ala Phe Leu Thr Met Leu  
325 330 335

Pro Arg Leu Glu Ile Leu Asp Leu Ser Phe Asn Tyr Ile Lys Gly Ser  
340 345 350

Tyr Pro Gln His Ile Asn Ile Ser Arg Asn Phe Ser Lys Leu Leu Ser  
355 360 365

Leu Arg Ala Leu His Leu Arg Gly Tyr Val Phe Gln Glu Leu Arg Glu  
370 375 380

Asp Asp Phe Gln Pro Leu Met Gln Leu Pro Asn Leu Ser Thr Ile Asn  
385 390 395 400

## 58182US002.ST25.txt

Leu Gly Ile Asn Phe Ile Lys Gln Ile Asp Phe Lys Leu Phe Gln Asn  
405 410 415

Phe Ser Asn Leu Glu Ile Ile Tyr Leu Ser Glu Asn Arg Ile Ser Pro  
420 425 430

Leu Val Lys Asp Thr Arg Gln Ser Tyr Ala Asn Ser Ser Ser Phe Gln  
435 440 445

Arg His Ile Arg Lys Arg Arg Ser Thr Asp Phe Glu Phe Asp Pro His  
450 455 460

Ser Asn Phe Tyr His Phe Thr Arg Pro Leu Ile Lys Pro Gln Cys Ala  
465 470 475 480

Ala Tyr Gly Lys Ala Leu Asp Leu Ser Leu Asn Ser Ile Phe Phe Ile  
485 490 495

Gly Pro Asn Gln Phe Glu Asn Leu Pro Asp Ile Ala Cys Leu Asn Leu  
500 505 510

Ser Ala Asn Ser Asn Ala Gln Val Leu Ser Gly Thr Glu Phe Ser Ala  
515 520 525

Ile Pro His Val Lys Tyr Leu Asp Leu Thr Asn Asn Arg Leu Asp Phe  
530 535 540

Asp Asn Ala Ser Ala Leu Thr Glu Leu Ser Asp Leu Glu Val Leu Asp  
545 550 555 560

Leu Ser Tyr Asn Ser His Tyr Phe Arg Ile Ala Gly Val Thr His His  
565 570 575

Leu Glu Phe Ile Gln Asn Phe Thr Asn Leu Lys Val Leu Asn Leu Ser  
580 585 590

His Asn Asn Ile Tyr Thr Leu Thr Asp Lys Tyr Asn Leu Glu Ser Lys  
595 600 605

Ser Leu Val Glu Leu Val Phe Ser Gly Asn Arg Leu Asp Ile Leu Trp  
610 615 620

Asn Asp Asp Asp Asn Arg Tyr Ile Ser Ile Phe Lys Gly Leu Lys Asn  
625 630 635 640

Leu Thr Arg Leu Asp Leu Ser Leu Asn Arg Leu Lys His Ile Pro Asn

## 58182US002.ST25.txt

645 650 655

Glu Ala Phe Leu Asn Leu Pro Ala Ser Leu Thr Glu Leu His Ile Asn  
660 665 670

Asp Asn Met Leu Lys Phe Phe Asn Trp Thr Leu Leu Gln Gln Phe Pro  
675 680 685

Arg Leu Glu Leu Leu Asp Leu Arg Gly Asn Lys Leu Leu Phe Leu Thr  
690 695 700

Asp Ser Leu Ser Asp Phe Thr Ser Ser Leu Arg Thr Leu Leu Leu Ser  
705 710 715 720

His Asn Arg Ile Ser His Leu Pro Ser Gly Phe Leu Ser Glu Val Ser  
725 730 735

Ser Leu Lys His Leu Asp Leu Ser Ser Asn Leu Leu Lys Thr Ile Asn  
740 745 750

Lys Ser Ala Leu Glu Thr Lys Thr Thr Lys Leu Ser Met Leu Glu  
755 760 765

Leu His Gly Asn Pro Phe Glu Cys Thr Cys Asp Ile Gly Asp Phe Arg  
770 775 780

Arg Trp Met Asp Glu His Leu Asn Val Lys Ile Pro Arg Leu Val Asp  
785 790 795 800

Val Ile Cys Ala Ser Pro Gly Asp Gln Arg Gly Lys Ser Ile Val Ser  
805 810 815

Leu Glu Leu Thr Thr Cys Val Ser Asp Val Thr Ala Val Ile Leu Phe  
820 825 830

Phe Phe Thr Phe Phe Ile Thr Thr Met Val Met Leu Ala Ala Leu Ala  
835 840 845

His His Leu Phe Tyr Trp Asp Val Trp Phe Ile Tyr Asn Val Cys Leu  
850 855 860

Ala Lys Val Lys Gly Tyr Arg Ser Leu Ser Thr Ser Gln Thr Phe Tyr  
865 870 875 880

Asp Ala Tyr Ile Ser Tyr Asp Thr Lys Asp Ala Ser Val Thr Asp Trp  
885 890 895

58182US002.ST25.txt

Val Ile Asn Glu Leu Arg Tyr His Leu Glu Glu Ser Arg Asp Lys Asn  
 900 905 910

Val Leu Leu Cys Leu Glu Glu Arg Asp Trp Asp Pro Gly Leu Ala Ile  
 915 920 925

Ile Asp Asn Leu Met Gln Ser Ile Asn Gln Ser Lys Lys Thr Val Phe  
 930 935 940

Val Leu Thr Lys Lys Tyr Ala Lys Ser Trp Asn Phe Lys Thr Ala Phe  
 945 950 955 960

Tyr Leu Ala Leu Gln Arg Leu Met Asp Glu Asn Met Asp Val Ile Ile  
 965 970 975

Phe Ile Leu Leu Glu Pro Val Leu Gln His Ser Gln Tyr Leu Arg Leu  
 980 985 990

Arg Gln Arg Ile Cys Lys Ser Ser Ile Leu Gln Trp Pro Asp Asn Pro  
 995 1000 1005

Lys Ala Glu Gly Leu Phe Trp Gln Thr Leu Arg Asn Val Val Leu  
 1010 1015 1020

Thr Glu Asn Asp Ser Arg Tyr Asn Asn Met Tyr Val Asp Ser Ile  
 1025 1030 1035

Lys Gln Tyr  
 1040

<210> 17  
 <211> 3352  
 <212> DNA  
 <213> Homo sapiens

<400> 17  
 aggctggat aaaaatctta cttcctctat tctctgagcc gctgctgccc ctgtggaaag 60  
 ggacctcgag tgtgaagcat cttccctgt agctgctgtc cagtctgccc gccagaccct 120  
 ctggagaagc ccctgcccc cagcatgggt ttctgcgcac gcgcctgca cccgctgtct 180  
 ctcctggtgc aggccatcat gctggccatg accctggccc tgggtacctt gcctgccttc 240  
 ctaccctgtg agctccagcc ccacggcctg gtgaactgca actggctgtt cctgaagtct 300  
 gtgccccact tctccatggc agcaccccggt ggcaatgtca ccagccttcc cttgtcctcc 360  
 aaccgcatcc accacctcca tgattctgac tttgccacc tgcccagcct gcggcatctc 420  
 aacctcaagt ggaactgccc gccgggtggc ctcagccccca tgcaattcccc ctgcccacatg 480  
 accatcgagc ccagcacctt cttggctgtg cccaccctgg aagagctaaa cctgagctac 540

## 58182US002.ST25.txt

aacaacatca	tgactgtgcc	tgcgctgccc	aaatccctca	tatccctgtc	cctcagccat	600	
accaacatcc	tgatgctaga	ctctgccagc	ctcgccggcc	tgcattccct	gcatgttcta	660	
ttcatggacg	gcaactgtta	ttacaagaac	ccctgcaggc	aggcactgga	ggtgtggcccg	720	
ggtgcctcc	ttggcctggg	caacctcacc	cacctgtcac	tcaagtacaa	caacctcact	780	
gtggtgcccc	gcaacctgcc	ttccagcctg	gagtatctgc	tgttgcctta	caaccgcac	840	
gtcaaaactgg	cgcctgagga	cctggccaat	ctgaccgccc	tgcgtgtgct	cgatgtggc	900	
ggaaattgcc	gccgctgcga	ccacgctccc	aacccctgca	tggagtgc	tcgtcacttc	960	
ccccagctac	atcccgatac	tttcagccac	ctgagccgtc	ttgaaggcct	ggtgttgaag	1020	
gacagttctc	tctcctggct	aatgcccagt	tggttccgtg	ggctgggaaa	cctccgagtg	1080	
ctggacctga	gtgagaactt	cctctacaaa	tgcattacta	aaaccaaggc	cttccaggc	1140	
ctaacacagc	tgcgcaagct	taacctgtcc	ttcaattacc	aaaagagggt	gtcctttgcc	1200	
cacctgtctc	tggcccttc	tttcgggagc	ctggtc	ccccat	tgaaggagct	ggacatgcac	1260
ggcatcttct	tccgctact	cgatgagacc	acgctccggc	cactggccc	cctgccc	1320	
ctccagactc	tgcgtctgca	gatgaacttc	atcaaccagg	cccagctcgg	catcttcagg	1380	
gcctccctg	gcctgcgcta	cgtggacctg	tcggacaacc	gcatcagcgg	agcttcggag	1440	
ctgacagCCA	ccatgggggA	ggcagatgga	ggggagaagg	tctggctgca	gcctggggac	1500	
cttgctccgg	ccccagtgg	cactcccagc	tctgaagact	tcaggccaa	ctgcagcacc	1560	
ctcaacttca	ccttggatct	gtcacggAAC	aacctggta	ccgtgcagcc	ggagatgttt	1620	
gcccagctct	cgcacctgca	gtgcctgcgc	ctgagccaca	actgcac	gcaggcagtc	1680	
aatggctccc	atggctgccc	gctgaccgg	ctgcagg	tgcac	tagacctgtc	ccgcaataag	1740
ctggacctct	accacgagca	ctcattcag	gagctaccgc	gactggaggc	cctggacctc	1800	
agctacaaca	gccagccctt	tggcatgcag	ggcgtggcc	acaacttcag	cttcgtggct	1860	
cacctgcgca	ccctgcgcca	cctcagcctg	gcccacaaca	acatccacag	ccaagtgtcc	1920	
cagcagctct	gcagtagcgc	gctgcgggccc	ctggacttca	gcccgaatgc	actggccat	1980	
atgtggccg	agggagacct	ctatctgcac	ttcttccaag	gcctgagcgg	tttgatctgg	2040	
ctggacttgt	cccagaaccg	cctgcacacc	ctcctgcccc	aaaccctg	caacccccc	2100	
aagagcctac	aggtgctgcg	tctccgtgac	aattacctgg	ccttctttaa	gtgggtggagc	2160	
ctccacttcc	tgcccaaact	ggaagtccctc	gacctggcag	gaaaccggct	gaaggccctg	2220	
accaatggca	gcctgcctgc	tggcacccgg	ctccggaggc	tggatgtcag	ctgcaacagc	2280	
atcagcttcg	tggcccccgg	cttctttcc	aaggccaagg	agctgcgaga	gctcaacctt	2340	
agcgccaacg	ccctcaagac	agtggaccac	tcctggttt	ggccctggc	gagtgcctg	2400	

58182US002.ST25.txt

caaatactag	atgtaagcgc	caaccctctg	caactgcgcct	gtggggcgcc	ctttatggac	2460
ttcctgctgg	aggtgtcaggc	tgcgcgtccc	ggtctgccc	gccgggtgaa	gtgtggcagt	2520
ccggggccagc	tccaggccct	cagcatctt	gcacaggacc	tgcgcctctg	cctggatgag	2580
gccctctcct	gggactgttt	cgcctctcg	ctgctggctg	tggctctggg	cctgggtgtg	2640
cccatgctgc	atcacctctg	tggctgggac	ctctggtaact	gcttccacct	gtgcctggcc	2700
tggcttcct	ggcggggcg	gcaaagtggg	cgagatgagg	atgcctgccc	ctacgatgcc	2760
ttcgtggtct	tcgacaaaac	gcagagcgc	gtggcagact	gggtgtacaa	cgagcttcgg	2820
gggcagctgg	aggagtgcgc	tggcgctgg	gcactccgccc	tgtgcctgg	ggaacgcgac	2880
tggctgcctg	gcaaaaccct	ctttgagaac	ctgtggccct	cggcttatgg	cagccgcaag	2940
acgctgtttg	tgctggccca	cacggacccgg	gtcagtggtc	tcttgcgcgc	cagcttcctg	3000
ctggcccgac	agcgcctgct	ggaggaccgc	aaggacgtcg	tggtgctgg	gatcctgagc	3060
cctgacggcc	gccgcctcccg	ctacgtgcgg	ctgcgcgc	gcctctgg	ccagagtgtc	3120
ctcctctggc	cccaccagcc	cagtggtcag	cgcagcttct	gggcccagct	gggcatggcc	3180
ctgaccaggg	acaaccacca	cttctataac	cgaaacttct	gccagggacc	cacggccgaa	3240
tagccgtgag	ccggaatcct	gcacggtgcc	acctccacac	tcacctcacc	tctgcctgccc	3300
tggtctgacc	ctccccctgct	cgcctccctc	accccacacc	tgacacagag	ca	3352

&lt;210&gt; 18

&lt;211&gt; 1032

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 18

Met	Gly	Phe	Cys	Arg	Ser	Ala	Leu	His	Pro	Leu	Ser	Leu	Leu	Val	Gln
1						5				10				15	

Ala	Ile	Met	Leu	Ala	Met	Thr	Leu	Ala	Leu	Gly	Thr	Leu	Pro	Ala	Phe
		20					25						30		

Leu	Pro	Cys	Glu	Leu	Gln	Pro	His	Gly	Leu	Val	Asn	Cys	Asn	Trp	Leu
		35				40					45				

Phe	Leu	Lys	Ser	Val	Pro	His	Phe	Ser	Met	Ala	Ala	Pro	Arg	Gly	Asn
				50			55			60					

Val	Thr	Ser	Leu	Ser	Leu	Ser	Ser	Asn	Arg	Ile	His	His	Leu	His	Asp
65					70				75				80		

Ser	Asp	Phe	Ala	His	Leu	Pro	Ser	Leu	Arg	His	Leu	Asn	Leu	Lys	Trp
					85			90				95			

## 58182US002.ST25.txt

Asn Cys Pro Pro Val Gly Leu Ser Pro Met His Phe Pro Cys His Met  
100 105 110

Thr Ile Glu Pro Ser Thr Phe Leu Ala Val Pro Thr Leu Glu Glu Leu  
115 120 125

Asn Leu Ser Tyr Asn Asn Ile Met Thr Val Pro Ala Leu Pro Lys Ser  
130 135 140

Leu Ile Ser Leu Ser Leu Ser His Thr Asn Ile Leu Met Leu Asp Ser  
145 150 155 160

Ala Ser Leu Ala Gly Leu His Ala Leu Arg Phe Leu Phe Met Asp Gly  
165 170 175

Asn Cys Tyr Tyr Lys Asn Pro Cys Arg Gln Ala Leu Glu Val Ala Pro  
180 185 190

Gly Ala Leu Leu Gly Leu Gly Asn Leu Thr His Leu Ser Leu Lys Tyr  
195 200 205

Asn Asn Leu Thr Val Val Pro Arg Asn Leu Pro Ser Ser Leu Glu Tyr  
210 215 220

Leu Leu Leu Ser Tyr Asn Arg Ile Val Lys Leu Ala Pro Glu Asp Leu  
225 230 235 240

Ala Asn Leu Thr Ala Leu Arg Val Leu Asp Val Gly Gly Asn Cys Arg  
245 250 255

Arg Cys Asp His Ala Pro Asn Pro Cys Met Glu Cys Pro Arg His Phe  
260 265 270

Pro Gln Leu His Pro Asp Thr Phe Ser His Leu Ser Arg Leu Glu Gly  
275 280 285

Leu Val Leu Lys Asp Ser Ser Leu Ser Trp Leu Asn Ala Ser Trp Phe  
290 295 300

Arg Gly Leu Gly Asn Leu Arg Val Leu Asp Leu Ser Glu Asn Phe Leu  
305 310 315 320

Tyr Lys Cys Ile Thr Lys Thr Lys Ala Phe Gln Gly Leu Thr Gln Leu  
325 330 335

Arg Lys Leu Asn Leu Ser Phe Asn Tyr Gln Lys Arg Val Ser Phe Ala  
340 345 350

## 58182US002.ST25.txt

His Leu Ser Leu Ala Pro Ser Phe Gly Ser Leu Val Ala Leu Lys Glu  
355 360 365

Leu Asp Met His Gly Ile Phe Phe Arg Ser Leu Asp Glu Thr Thr Leu  
370 375 380

Arg Pro Leu Ala Arg Leu Pro Met Leu Gln Thr Leu Arg Leu Gln Met  
385 390 395 400

Asn Phe Ile Asn Gln Ala Gln Leu Gly Ile Phe Arg Ala Phe Pro Gly  
405 410 415

Leu Arg Tyr Val Asp Leu Ser Asp Asn Arg Ile Ser Gly Ala Ser Glu  
420 425 430

Leu Thr Ala Thr Met Gly Glu Ala Asp Gly Gly Glu Lys Val Trp Leu  
435 440 445

Gln Pro Gly Asp Leu Ala Pro Ala Pro Val Asp Thr Pro Ser Ser Glu  
450 455 460

Asp Phe Arg Pro Asn Cys Ser Thr Leu Asn Phe Thr Leu Asp Leu Ser  
465 470 475 480

Arg Asn Asn Leu Val Thr Val Gln Pro Glu Met Phe Ala Gln Leu Ser  
485 490 495

His Leu Gln Cys Leu Arg Leu Ser His Asn Cys Ile Ser Gln Ala Val  
500 505 510

Asn Gly Ser Gln Phe Leu Pro Leu Thr Gly Leu Gln Val Leu Asp Leu  
515 520 525

Ser Arg Asn Lys Leu Asp Leu Tyr His Glu His Ser Phe Thr Glu Leu  
530 535 540

Pro Arg Leu Glu Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro Phe Gly  
545 550 555 560

Met Gln Gly Val Gly His Asn Phe Ser Phe Val Ala His Leu Arg Thr  
565 570 575

Leu Arg His Leu Ser Leu Ala His Asn Asn Ile His Ser Gln Val Ser  
580 585 590

Gln Gln Leu Cys Ser Thr Ser Leu Arg Ala Leu Asp Phe Ser Gly Asn  
Page 45

58182US002.ST25.txt  
595            600            605

Ala Leu Gly His Met Trp Ala Glu Gly Asp Leu Tyr Leu His Phe Phe  
610            615            620

Gln Gly Leu Ser Gly Leu Ile Trp Leu Asp Leu Ser Gln Asn Arg Leu  
625            630            635            640

His Thr Leu Leu Pro Gln Thr Leu Arg Asn Leu Pro Lys Ser Leu Gln  
645            650            655

Val Leu Arg Leu Arg Asp Asn Tyr Leu Ala Phe Phe Lys Trp Trp Ser  
660            665            670

Leu His Phe Leu Pro Lys Leu Glu Val Leu Asp Leu Ala Gly Asn Arg  
675            680            685

Leu Lys Ala Leu Thr Asn Gly Ser Leu Pro Ala Gly Thr Arg Leu Arg  
690            695            700

Arg Leu Asp Val Ser Cys Asn Ser Ile Ser Phe Val Ala Pro Gly Phe  
705            710            715            720

Phe Ser Lys Ala Lys Glu Leu Arg Glu Leu Asn Leu Ser Ala Asn Ala  
725            730            735

Leu Lys Thr Val Asp His Ser Trp Phe Gly Pro Leu Ala Ser Ala Leu  
740            745            750

Gln Ile Leu Asp Val Ser Ala Asn Pro Leu His Cys Ala Cys Gly Ala  
755            760            765

Ala Phe Met Asp Phe Leu Leu Glu Val Gln Ala Ala Val Pro Gly Leu  
770            775            780

Pro Ser Arg Val Lys Cys Gly Ser Pro Gly Gln Leu Gln Gly Leu Ser  
785            790            795            800

Ile Phe Ala Gln Asp Leu Arg Leu Cys Leu Asp Glu Ala Leu Ser Trp  
805            810            815

Asp Cys Phe Ala Leu Ser Leu Leu Ala Val Ala Leu Gly Leu Gly Val  
820            825            830

Pro Met Leu His His Leu Cys Gly Trp Asp Leu Trp Tyr Cys Phe His  
835            840            845

## 58182us002.ST25.txt

Leu Cys Leu Ala Trp Leu Pro Trp Arg Gly Arg Gln Ser Gly Arg Asp  
 850 855 860 860  
  
 Glu Asp Ala Leu Pro Tyr Asp Ala Phe Val Val Phe Asp Lys Thr Gln  
 865 870 875 880 880  
  
 Ser Ala Val Ala Asp Trp Val Tyr Asn Glu Leu Arg Gly Gln Leu Glu  
 885 890 895 895  
  
 Glu Cys Arg Gly Arg Trp Ala Leu Arg Leu Cys Leu Glu Glu Arg Asp  
 900 905 910 910  
  
 Trp Leu Pro Gly Lys Thr Leu Phe Glu Asn Leu Trp Ala Ser Val Tyr  
 915 920 925 925  
  
 Gly Ser Arg Lys Thr Leu Phe Val Leu Ala His Thr Asp Arg Val Ser  
 930 935 940 940  
  
 Gly Leu Leu Arg Ala Ser Phe Leu Leu Ala Gln Gln Arg Leu Leu Glu  
 945 950 955 960 960  
  
 Asp Arg Lys Asp Val Val Val Leu Val Ile Leu Ser Pro Asp Gly Arg  
 965 970 975 975  
  
 Arg Ser Arg Tyr Val Arg Leu Arg Gln Arg Leu Cys Arg Gln Ser Val  
 980 985 990 990  
  
 Leu Leu Trp Pro His Gln Pro Ser Gly Gln Arg Ser Phe Trp Ala Gln  
 995 1000 1005 1005  
  
 Leu Gly Met Ala Leu Thr Arg Asp Asn His His Phe Tyr Asn Arg  
 1010 1015 1020 1020  
  
 Asn Phe Cys Gln Gly Pro Thr Ala Glu  
 1025 1030 1030  
  
 <210> 19  
 <211> 3002  
 <212> DNA  
 <213> Homo sapiens  
  
 <400> 19  
 gtggcttgggt attcactggc aggtttcaga cattagatc tttcttttaa tgactaacac 60  
 catgcctatc tgtggagaag ctggcaacat gtcacacctg gaaattgttt ttcaacattt 120  
 atactattat ttggcagtaa tccagattgc tttgccacc aacctgaaga catatagagg 180  
 cagaaggaca ggaataattc tatttgttgc ctgtttgaa acttccatct gtaaggctat 240  
 caaaaggaga tgtgagagag ggtattgagt ctggccgtac aatgcagttc ttaaacaaaa 300

## 58182US002.ST25.txt

ggtccattat gcttctcctc tctgagaatc ctgacttacc tcaacaacgg agacatggca	360
cagtagccag cttggagact tctcagccaa tgctctgaga tcaagtcgaa gacccaatat	420
acagggtttt gagctcatct tcattcattca tatgaggaaa taagtggtaa aatccttgaa	480
aatacaatga gactcatcag aaacatttac atatttgtt gtattgtt gacagcagag	540
ggtgatgctc cagagctgcc agaagaaagg gaactgatga ccaactgctc caacatgtct	600
ctaagaaagg ttccccgaga cttgacccca gccacaacga cactggattt atcctataac	660
ctcccttttc aactccagag ttcagattt cattctgtct ccaaactgag agttttgattt	720
ctatgccata acagaattca acagctggat ctcaaaacct ttgaattcaa caaggagttt	780
agatatttag atttgtctaa taacagactg aagagtgtaa cttggatttt actggcaggt	840
ctcaggtatt tagatcttc ttttaatgac tttgacacca tgcctatctg tgaggaagct	900
ggcaacatgt cacacctgga aatcctagg ttagtgggg caaaaataca aaaatcagat	960
ttccagaaaa ttgctcatct gcatctaaat actgtttct taggattcag aactcttcct	1020
cattatgaag aaggttagcct gcccatttta aacacaacaa aactgcacat tgttttacca	1080
atggacacaa atttctgggt tctttgcgt gatggaatca agacttcaaa aatatttagaa	1140
atgacaata tagatggcaa aagccaattt gtaagttatg aaatgcaacg aaatcttagt	1200
ttagaaaatg ctaagacatc gtttctattt cttataaaat ttgatttact ctgggacgac	1260
cttttcctta tcttacaatt tttttggcat acatcagtgg aacactttca gatccgaaat	1320
gtgacttttgcgtt ggtaaggc ttatcttgcac cacaattcat ttgactactc aaatactgt	1380
atgagaacta taaaatttggaa gcatgtacat ttcagagtgt tttacattca acaggataaa	1440
atctatttgc ttttgcacaa aatggacata gaaaacctga caatatcaaa tgcacaaatg	1500
ccacacatgc ttttccgaa ttatcctacg aaattccaaat atttaaattt tgccaataat	1560
atcttaacatgc acgagttgtt taaaagaact atccaaatgc ctcacttgaa aactctcatt	1620
ttgaatggca ataaaacttggaa gacactttct ttagtaagtt gctttgctaa caacacaccc	1680
ttggAACACT tggatctgag tcaaaatcta ttacaacata aaaatgtga aaattgctca	1740
tggccagaaa ctgtggtcaa tatgaatctg tcatacata aattgtctga ttctgtcttc	1800
aggtgcttgc ccaaaagtat tcaaatactt gacctaata ataaccaaata ccaaactgtat	1860
cctaaagaga ctattcatct gatggcctta cgagaactaa atattgcatt taattttcta	1920
actgatctcc ctggatgcag tcatttcagt agactttcag ttctgaacat taaaatgtac	1980
ttcattctca gcccattctct ggattttgtt cagagctgcc aggaagttaa aactctaaat	2040
gcgggaagaa atccattccg gtgtacctgtt gaattaaaaa atttcattca gcttggaaaca	2100
tattcagagg tcatgtatgtt tggatggtca gattcatacata cctgtgaata ccctttaaac	2160

58182US002.ST25.txt

ctaagggaa	ttaggtaaa	agacgttcat	ctccacgaat	tatcttgcaa	cacagctctg	2220
ttgattgtca	ccattgtggt	tattatgcta	gttctgggt	tggctgtggc	cttctgctgt	2280
ctccacttg	atctgccctg	gtatctcagg	atgcttaggtc	aatgcacaca	aacatggcac	2340
agggttagga	aaacaaccca	agaacaactc	aagagaaaatg	tccgattcca	cgcatttatt	2400
tcatacagt	aacatgattc	tctgtgggt	aagaatgaat	tgatccccaa	tctagagaag	2460
gaagatgggt	ctatcttgat	ttgcctttat	gaaagctact	ttgaccctgg	caaaagcatt	2520
agtgaaaata	ttgtaagctt	cattgagaaa	agctataagt	ccatctttgt	tttgtctccc	2580
aactttgtcc	agaatgagtg	gtgccattat	gaatttact	ttgcccacca	caatctcttc	2640
catgaaaatt	ctgatcatat	aattcttatac	ttactggaac	ccattccatt	ctattgcatt	2700
ccaccagg	atcataaact	gaaagctctc	ctggaaaaaa	aagcatactt	ggaatggccc	2760
aaggataggc	gtaaatgtgg	gctttctgg	gcaaacccttc	gagctgctat	taatgttaat	2820
gtattagcca	ccagagaaaat	gtatgaactg	cagacattca	cagagttaaa	tgaagagtct	2880
cgaggttcta	caatctct	gatgagaaca	gattgtctat	aaaatcccac	agtccttggg	2940
aagttgggga	ccacatacac	tgttgggatg	tacattgata	caacccttat	gatggcaatt	3000
tg						3002

<210> 20  
<211> 811  
<212> PRT  
<213> Homo sapiens  
<400> 20

Met Arg Leu Ile Arg Asn Ile Tyr Ile Phe Cys Ser Ile Val Met Thr  
1                       5                                   10                           15

Ala Glu Gly Asp Ala Pro Glu Leu Pro Glu Glu Arg Glu Leu Met Thr  
20                      25                                   30

Asn Cys Ser Asn Met Ser Leu Arg Lys Val Pro Ala Asp Leu Thr Pro  
35                      40                                   45

Ala Thr Thr Thr Leu Asp Leu Ser Tyr Asn Leu Leu Phe Gln Leu Gln  
50                      55                                   60

Ser Ser Asp Phe His Ser Val Ser Lys Leu Arg Val Leu Ile Leu Cys  
65                      70                                   75                           80

His Asn Arg Ile Gln Gln Leu Asp Leu Lys Thr Phe Glu Phe Asn Lys  
85                      90                                   95

Glu Leu Arg Tyr Leu Asp Leu Ser Asn Asn Arg Leu Lys Ser Val Thr  
Page 49

58182US002.ST25.txt  
100                    105                    110

Trp Tyr Leu Leu Ala Gly Leu Arg Tyr Leu Asp Leu Ser Phe Asn Asp  
115                    120                    125

Phe Asp Thr Met Pro Ile Cys Glu Glu Ala Gly Asn Met Ser His Leu  
130                    135                    140

Glu Ile Leu Gly Leu Ser Gly Ala Lys Ile Gln Lys Ser Asp Phe Gln  
145                    150                    155                    160

Lys Ile Ala His Leu His Leu Asn Thr Val Phe Leu Gly Phe Arg Thr  
165                    170                    175

Leu Pro His Tyr Glu Glu Gly Ser Leu Pro Ile Leu Asn Thr Thr Lys  
180                    185                    190

Leu His Ile Val Leu Pro Met Asp Thr Asn Phe Trp Val Leu Leu Arg  
195                    200                    205

Asp Gly Ile Lys Thr Ser Lys Ile Leu Glu Met Thr Asn Ile Asp Gly  
210                    215                    220

Lys Ser Gln Phe Val Ser Tyr Glu Met Gln Arg Asn Leu Ser Leu Glu  
225                    230                    235                    240

Asn Ala Lys Thr Ser Val Leu Leu Leu Asn Lys Val Asp Leu Leu Trp  
245                    250                    255

Asp Asp Leu Phe Leu Ile Leu Gln Phe Val Trp His Thr Ser Val Glu  
260                    265                    270

His Phe Gln Ile Arg Asn Val Thr Phe Gly Gly Lys Ala Tyr Leu Asp  
275                    280                    285

His Asn Ser Phe Asp Tyr Ser Asn Thr Val Met Arg Thr Ile Lys Leu  
290                    295                    300

Glu His Val His Phe Arg Val Phe Tyr Ile Gln Gln Asp Lys Ile Tyr  
305                    310                    315                    320

Leu Leu Leu Thr Lys Met Asp Ile Glu Asn Leu Thr Ile Ser Asn Ala  
325                    330                    335

Gln Met Pro His Met Leu Phe Pro Asn Tyr Pro Thr Lys Phe Gln Tyr  
340                    345                    350

58182US002.ST25.txt

Leu Asn Phe Ala Asn Asn Ile Leu Thr Asp Glu Leu Phe Lys Arg Thr  
355 360 365

Ile Gln Leu Pro His Leu Lys Thr Leu Ile Leu Asn Gly Asn Lys Leu  
370 375 380

Glu Thr Leu Ser Leu Val Ser Cys Phe Ala Asn Asn Thr Pro Leu Glu  
385 390 395 400

His Leu Asp Leu Ser Gln Asn Leu Leu Gln His Lys Asn Asp Glu Asn  
405 410 415

Cys Ser Trp Pro Glu Thr Val Val Asn Met Asn Leu Ser Tyr Asn Lys  
420 425 430

Leu Ser Asp Ser Val Phe Arg Cys Leu Pro Lys Ser Ile Gln Ile Leu  
435 440 445

Asp Leu Asn Asn Asn Gln Ile Gln Thr Val Pro Lys Glu Thr Ile His  
450 455 460

Leu Met Ala Leu Arg Glu Leu Asn Ile Ala Phe Asn Phe Leu Thr Asp  
465 470 475 480

Leu Pro Gly Cys Ser His Phe Ser Arg Leu Ser Val Leu Asn Ile Glu  
485 490 495

Met Asn Phe Ile Leu Ser Pro Ser Leu Asp Phe Val Gln Ser Cys Gln  
500 505 510

Glu Val Lys Thr Leu Asn Ala Gly Arg Asn Pro Phe Arg Cys Thr Cys  
515 520 525

Glu Leu Lys Asn Phe Ile Gln Leu Glu Thr Tyr Ser Glu Val Met Met  
530 535 540 540

Val Gly Trp Ser Asp Ser Tyr Thr Cys Glu Tyr Pro Leu Asn Leu Arg  
545 550 555 560

Gly Ile Arg Leu Lys Asp Val His Leu His Glu Leu Ser Cys Asn Thr  
565 570 575

Ala Leu Leu Ile Val Thr Ile Val Val Ile Met Leu Val Leu Gly Leu  
580 585 590

Ala Val Ala Phe Cys Cys Leu His Phe Asp Leu Pro Trp Tyr Leu Arg  
595 600 605

## 58182US002.ST25.txt

Met Leu Gly Gln Cys Thr Gln Thr Trp His Arg Val Arg Lys Thr Thr  
 610 615 620

Gln Glu Gln Leu Lys Arg Asn Val Arg Phe His Ala Phe Ile Ser Tyr  
 625 630 635 640

Ser Glu His Asp Ser Leu Trp Val Lys Asn Glu Leu Ile Pro Asn Leu  
 645 650 655

Glu Lys Glu Asp Gly Ser Ile Leu Ile Cys Leu Tyr Glu Ser Tyr Phe  
 660 665 670

Asp Pro Gly Lys Ser Ile Ser Glu Asn Ile Val Ser Phe Ile Glu Lys  
 675 680 685

Ser Tyr Lys Ser Ile Phe Val Leu Ser Pro Asn Phe Val Gln Asn Glu  
 690 695 700

Trp Cys His Tyr Glu Phe Tyr Phe Ala His His Asn Leu Phe His Glu  
 705 710 715 720

Asn Ser Asp His Ile Ile Leu Ile Leu Leu Glu Pro Ile Pro Phe Tyr  
 725 730 735

Cys Ile Pro Thr Arg Tyr His Lys Leu Lys Ala Leu Leu Glu Lys Lys  
 740 745 750

Ala Tyr Leu Glu Trp Pro Lys Asp Arg Arg Lys Cys Gly Leu Phe Trp  
 755 760 765

Ala Asn Leu Arg Ala Ala Ile Asn Val Asn Val Leu Ala Thr Arg Glu  
 770 775 780

Met Tyr Glu Leu Gln Thr Phe Thr Glu Leu Asn Glu Glu Ser Arg Gly  
 785 790 795 800

Ser Thr Ile Ser Leu Met Arg Thr Asp Cys Leu  
 805 810

<210> 21

<211> 215

<212> DNA

<213> Homo sapiens

<400> 21

aaaaacaaaa catttgagaa acacggctct aaactcatgt aaagagtgc tgaaggaaag

60

caaaaacaga aatgaaaagt gccccagaag cattaagaaa gtggaaatca gtatgttccc

120

58182US002.ST25.txt  
tatttaaggc atttgcagga agcaaggcct tcagagaacc tagagccaa ggttcagagt 180  
cacccatctc agcaagccca gaagtatctg caata 215

<210> 22  
<211> 36  
<212> DNA  
<213> Artificial

<220>  
<223> 5' primer for human IFN-alpha promoter

<400> 22  
acgagatcta agctaaaaac aaaacatttg agaaac 36

<210> 23  
<211> 28  
<212> DNA  
<213> Artificial

<220>  
<223> 3' primer for human IFN-alpha promoter

<400> 23  
acgagatcta gatattgcag atacttct 28